DEPARTMENTS OF LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES APPROPRIATIONS FOR FISCAL YEAR 2008

MONDAY, MAY 21, 2007

U.S. SENATE,
SUBCOMMITTEE OF THE COMMITTEE ON APPROPRIATIONS,
Washington, DC.

The subcommittee met at 2 p.m., in room SD–116, Dirksen Senate Office Building, Hon. Tom Harkin (chairman) presiding.

Present: Senators Harkin, Cochran, and Stevens.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

STATEMENT OF DR. ANTHONY S. FAUCI, DIRECTOR, NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

OPENING STATEMENT OF SENATOR TOM HARKIN

Senator HARKIN. The Subcommittee on Labor, Health and Human Services, and Education, and Related Agencies will come to order.

I just thought that before we begin today's hearing I want to take a moment to offer my condolences to everyone, through you, at NIH over the recent passing of Dr. Steve Straus, the founding Director of the National Center for Complementary and Alternative Medicine. It's an enormous loss to science and to his many friends and colleagues at NIH where he worked for 27 years. We always knew that Steve was a man of great integrity and skill and dedication. That was apparent from his many scientific accomplishments.

But during his 2½ year battle with brain cancer we also witnessed his courage and his grace. He fought a valiant fight and was a teacher until the end. We were lucky to have him as NCCAM's founding director.

He and I had many, many conversations and meetings on alternative medicine, complementary medicine, where we're going and how we fold that in with other mainstream research. I think he's one of those people of whom we can truly say that he did make the world a better place.

So, this is the fifth of six hearings on the National Institutes of Health that the subcommittee will hold this year. We've heard from 13 Institutes so far. Today we'll hear from five more: the National Institute of Allergy and Infectious Diseases, the National Cancer

Institute, the National Center for Research Resources, the National Institute of Nursing Research and the National Center on Minority Health and Health Disparities.

I'll ask each Director to speak 5 to 7 minutes. In the spirit of how we've been doing this if I think of something while you're doing it I may even ask you a question at that time or—I excuse myself right now for interrupting. But we'll try to go through all of the testimonies and we'll just open up for general discussion after that.

I kind of like this format a little bit more than the formal one of sitting at a dais and that type of thing. I'd rather have more of a free flow of a discussion, sometimes even amongst you sitting across the table from me.

I think we learn a lot more and we get a better flavor for exactly what we're doing here. I know that C-SPAN and others pick this up. I look upon this as a way of also of teaching the public, getting information out to the public in a format in which they can get a better handle on just exactly what NIH is doing and what the different Institutes are doing.

So with that I'll start us here on my left. Dr. Anthony Fauci has served as Director of the National Institute of Allergy and Infectious Diseases since 1984. He received his MD degree from Cornell University Medical College. He has testified before this subcommittee many, many times over the years on everything from AIDS to pandemic flu to bioterrorism. I took over the Chair of the subcommittee in 1989. That was the first time I met Dr. Fauci.

So, welcome back, Dr. Fauci. All your statements will be made a part of the record in their entirety. Like I said if you could take 5 to 7 minutes or so, sum it up. I'd sure appreciate it.

SUMMARY STATEMENT OF DR. ANTHONY S. FAUCI

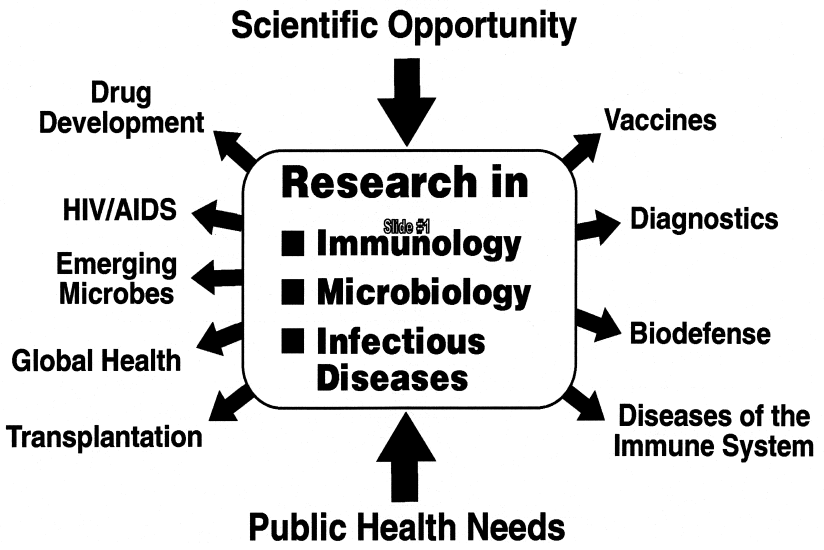
Dr. FAUCI. Thank you very much, Mr. Chairman and thank you for the opportunity to talk to you today a little bit about the activities of the National Institute of Allergy and Infectious Diseases.

I'm going to talk from some visuals that are right in front of you—right in front of you there.

Senator HARKIN. Okay.

Dr. FAUCI. I believe that's the top one. If you turn the page and look at the first slide.

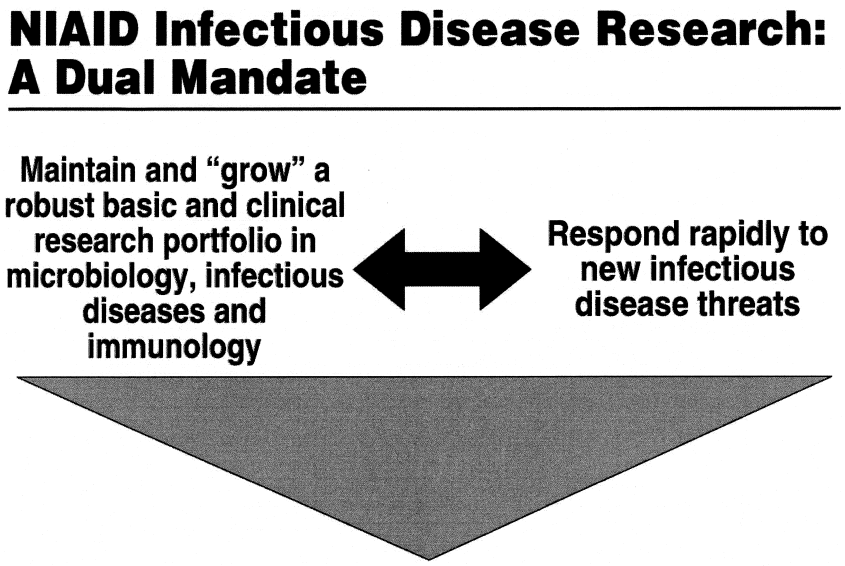
National Institute of Allergy and Infectious Diseases (NIAID)
National Institutes of Health (NIH)



I want to use that to tell you something that I know that you're familiar with. But for the sake of the record I will just mention very briefly what the mandate and the mission of the National Institute of Allergy and Infectious Diseases is. As you know it's responsible for the bulk of NIH research in the disciplines of immunology, microbiology and infectious diseases.

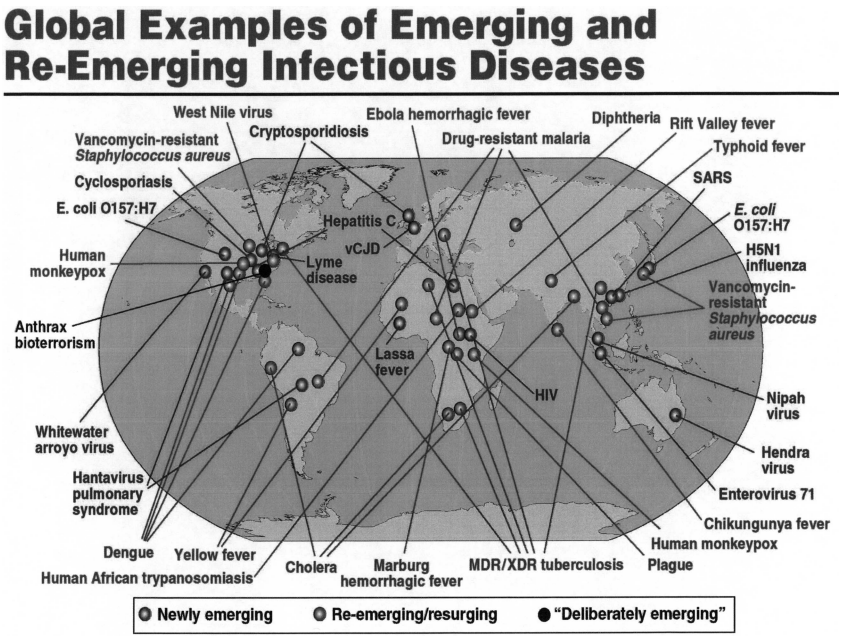
We're driven by two major issues. One is the scientific opportunity and the other is the public health need. You know about what we do from the much publicized issues such as HIV/AIDS, pandemic influenza and bio-defense. But we also have responsibility for emerging/re-emerging microbes, vaccinations and immunizations for adults and children, the development of antibiotics, vaccines as well as the study of diseases of the immune system, including the important issue of immunological tolerance, which has a great potential in many areas of medicine that go well beyond our Institute's mandate.

If you look at the next slide—I talk also here about what I call the dual mandate. Because in addition to all that we do, as every other Institute does, maintain a robust, basic and clinical research portfolio. For us it's microbiology, infectious diseases and the immune system. For Dr. Niederhuber, it's cancer and down the line. They each have what they do and what their Institute is responsible for.



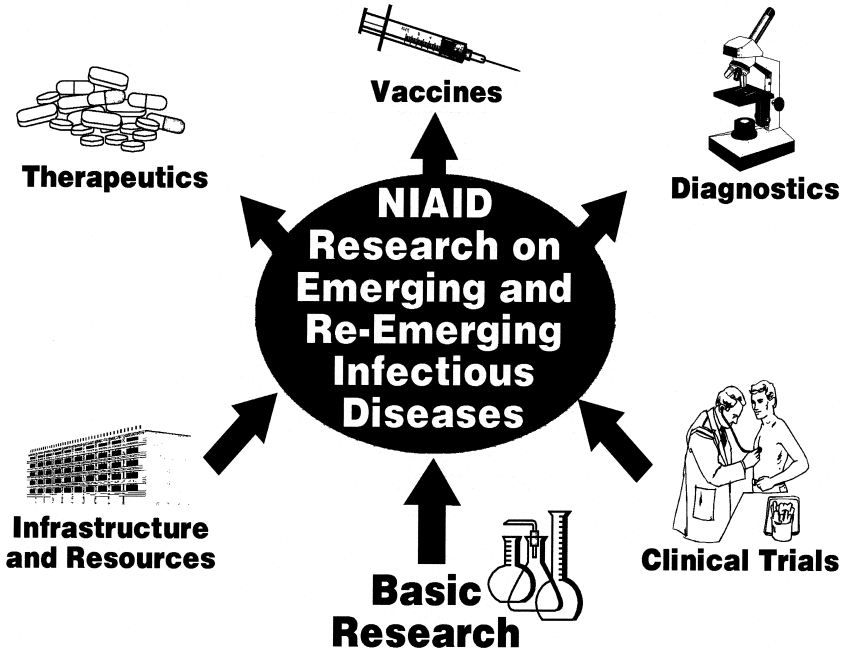
When I refer to our dual mandate I mean that we also need to be able to respond very rapidly to new infectious disease threats. You know we've discussed this at many hearings that we've had together on issues such as: HIV/AIDS, SARS, et cetera.

In fact if you go to the next slide. This is a slide I must have shown to you, Mr. Chairman, over the years since 1989 about 10 different times. The reason I can show you this—I hope without your getting bored, is that each year we add one, two and sometimes three, new emerging infectious diseases. In fact the print has gotten so small there that we're sort of running out of space. We started out with HIV/AIDS there, but you see there are many others that are emerging and re-emerging infectious diseases.



Of particular note this time is one that we've just recently added, which I hope we get a chance to discuss in the question period. That is extensively drug resistant tuberculosis, which is an issue that poses a significant threat to us. Also there are multiple drug resistant microbes like staphylococcus and enterococcus as well as things like the E. coli contamination of our spinach and our lettuce that was a major challenge just some months ago.

If you go to the next slide it really describes schematically, how we accomplish this. The NIAID research, for example on emerging and re-emerging infectious diseases is, as with all Institutes, based on a fundamental matrix of basic research which we hopefully then apply to the things that we need to do for the American public. In our case, it's the development of countermeasures, for example, in the forms of diagnostics, therapeutics and vaccines.



What I'd like to do in the next couple of slides is just go over with you some of the selected accomplishments which are also selected opportunities. So I'll go through them rapidly with you. If you look at HIV/AIDS, there has been this year, in addition to the great accomplishments of drugs that have essentially transformed the lives of HIV infected individuals. We know now that there have been a total, in a conservative estimate of about 3 million years of life saved in the United States on the basis of the anti-HIV therapeutic regimens that have been used.

Emerging/Re-Emerging Infectious Diseases: Selected Opportunities

HIV/AIDS

- New generation of anti-HIV drugs
- Expanded HIV vaccine trials
- New tools for HIV prevention, e.g. microbicides and circumcision

Malaria

- Mining genomic sequences of parasite and vector
- Averting and overcoming drug resistance
- Novel vaccine candidates

Influenza

- Development of new countermeasures for both seasonal and pandemic influenza, e.g. vaccines, therapeutics, and diagnostics

This year we have a couple of new drugs that are very exciting and will in fact, even improve that menu of drugs that we have available. In addition we have expanded HIV vaccine trials that we have embarked upon: one in collaboration with Merck and one with the Vaccine Research Center at the National Institutes of Health. In addition there are new tools for improvement such as the announcement that you probably heard of a few months ago about the protective effect of medically supervised adult circumcision for the prevention of HIV infection.

If you move on to malaria there have been some exciting new issues that have come up. For example, the sequencing of the parasite itself, and at least two or three of the vectors, namely the mosquitoes that cause it, allow us to get a greater insight into transmissibility, as well as drug resistance to the standard malaria antiparasitic drugs.

In influenza we're pleased to mention to you something that was announced just a short time ago, is that at our last hearing I mentioned to you that we were in the process of developing a pre-pandemic influenza vaccine. Just last month the FDA has approved that as an approved vaccine. We still need to make better vaccines for pandemic flu but we have at least one that's approved by the FDA.

UNIVERSAL INFLUENZA VACCINE

Senator HARKIN. That's not a universal?

Dr. FAUCI. No, no. We'll get to that, hopefully, in the questions. This isn't a universal—this is for the H5N1 bird flu.

Senator HARKIN. Specifically.

Dr. FAUCI. Specifically for the bird flu.

Then on the next slide I mention tuberculosis. I mentioned in my very earlier comments the real threat that we're seeing with this extensively drug resistant tuberculosis. NIAID has developed a strategic plan, very rapidly, which just this morning, at our National Advisory Council was presented to them for their final comments before we actually make it public. We'd be happy to provide that to you and your staff if you'd like it.

Emerging/Re-Emerging Infectious Diseases: Selected Opportunities

Tuberculosis

- Additional drug and vaccine candidates in clinical trials
- Development of point-of-care diagnostics
- Implementation of NIAID research agenda for XDR-TB

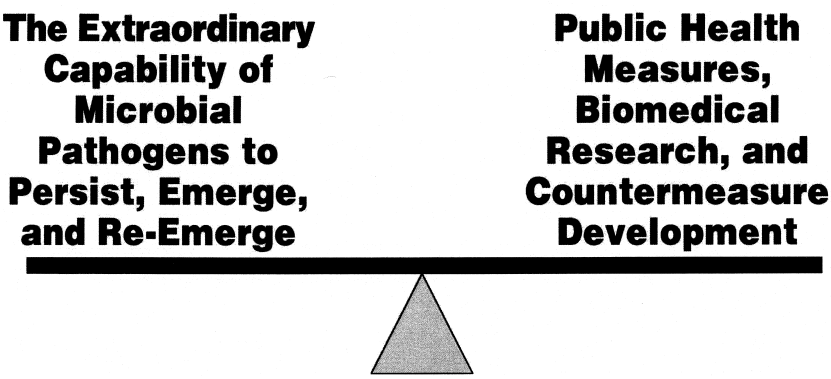
Potential Bioterror Agents

- Enhanced research infrastructure
- Application of basic research findings to the development of countermeasures

Then finally potential bio-terror agents, we've enhanced the infrastructure. Again a year or two ago I showed you the blueprints for the physical infrastructure that we were going to do. Several of those buildings are either near completion or actually up or—and operational such as the building on the NIH campus, building 33.

So if we go now to the last slide. I just want to close by saying that I've been talking to you about the threats of emerging and re-emerging infections and how the NIH research endeavor can meet these challenges, hopefully. I refer to it on this slide as a perpetual challenge because microbes will continue to emerge and re-emerge and nothing that we can do because of their evolutionary capability is going to allow us to completely eliminate the threat.

A Delicate Balance: The Perpetual Challenge



PREPARED STATEMENT

Dr. FAUCI. The best that we can do and I think it's something very important, is to maintain that balance by a very robust, research portfolio that can be wedded to our public health endeavors. We appreciate you and the committee for the support that you've given us over so many years. Thank you very much.

[The statement follows:]

PREPARED STATEMENT OF DR. ANTHONY S. FAUCI

Mr. Chairman and Members of the Committee: I am pleased to present the President's budget request for the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH). The fiscal year 2008 budget includes $4,592,482,000.

The mission of NIAID is to conduct and support research to understand, treat, and prevent infectious and immune-mediated diseases. Infectious diseases include well-known killers such as HIV/AIDS, malaria, tuberculosis, lower respiratory infections and diarrheal illnesses; naturally emerging or re-emerging threats such as pandemic influenza and SARS; and "deliberately emerging" threats from potential agents of bioterrorism. Preemptive medicine, in the form of vaccines and other prevention tools, is a major focus of the NIAID research portfolio in infectious diseases. Immune-mediated disorders include autoimmune diseases such as type 1 diabetes, lupus, and rheumatoid arthritis as well as asthma, allergies, and problems associated with transplanted tissues and organs. Here again, preemptive medicine is an important component of our research efforts, as NIAID extramural scientists work to predict, prevent, and treat immune-mediated diseases more effectively.

The NIAID mission has two distinct mandates. First, NIAID must plan and execute a comprehensive, long-term program of basic and clinical research on well-recognized endemic infectious and immune-mediated diseases. Second—and in this case distinctive among the NIH Institutes—NIAID must respond quickly with targeted research to meet new and unexpected infectious disease threats as they arise, often in the form of public health emergencies.

EMERGING AND RE-EMERGING INFECTIOUS DISEASES

Despite advances in medicine and public health such as antibiotics, vaccines, and improved sanitation, the World Health Organization (WHO) estimates that infec-

tious diseases still account for approximately 26 percent of all deaths worldwide, including about two-thirds of all deaths among children younger than 5 years of age. Moreover, the pathogens we face are not static, but change dramatically over time as new microbes emerge and familiar ones re-emerge with new properties or in unusual settings.

Influenza is a classic example of a re-emerging disease. Because circulating human influenza viruses continually accumulate small changes, a new vaccine must be made for each influenza season. When an influenza virus emerges that has undergone a major genetic shift such that the global population has limited natural immunity but the virus can be easily transmitted among people, a worldwide pandemic can result. Three influenza pandemics occurred in the 20th century, including the 1918 pandemic that killed more than 50 million people worldwide.

It is imperative that we take a preemptive approach to the possibility that a new influenza virus will emerge to cause a 1918-like pandemic. How well we do that, however, depends to a large extent on improving how we cope with seasonal influenza, which kills an average of about 36,000 people in the United States each year. Control of both seasonal and pandemic influenza requires development of and access to a sufficient supply of effective vaccines and antiviral drugs, effective infection control measures, and clear public communication. In this regard, NIAID research has directly laid the foundation for improved influenza vaccine manufacturing methods, new categories of vaccines that may work against multiple influenza strains, and the next generation of anti-influenza drugs. Certain of these goals will be accomplished through basic research projects intended to increase our understanding of how animal and human influenza viruses replicate, interact with their hosts, stimulate immune responses, and evolve into new strains. Other goals will be accomplished through targeted projects, such as a program to screen compounds for antiviral activity against influenza viruses.

Since last year, we have made substantial progress in influenza vaccine research. The inactivated-virus H5N1 vaccine currently stockpiled by the Department of Health and Human Services has been shown in NIAID-sponsored clinical trials to be safe and capable of inducing an immune response predictive of being protective against the H5N1 virus in healthy adults, children, and seniors. Although the vaccine dose required to induce this response is high, studies on enhancing the immune response to lower doses by employing immune enhancers called adjuvants are showing promising preliminary results. NIAID also is collaborating with industry to pursue several other vaccine strategies in addition to inactivated virus H5N1 vaccines. For example, trials of cold-adapted, live-attenuated H5N1 vaccine candidates are underway, as is a Phase I clinical test of a novel DNA H5N1 vaccine candidate developed at the NIAID Vaccine Research Center.

We also have made progress in antiviral drug and diagnostic test research over the past year. An NIAID program that screens both licensed drugs and new drug candidates—first in cell culture systems and then in animal models—has identified several promising anti-influenza candidates that are now being further developed in partnership with industry sponsors. These include FluDase, which binds host cell receptors to prevent viral entry; T–705, which inhibits replication of viral RNA; and Peramavir, which inhibits an influenza enzyme called neuraminidase. Research into influenza diagnostics is being vigorously pursued. For example, NIAID-funded researchers, working in collaboration with scientists at the Centers for Disease Control and Prevention, have reported encouraging results with a potentially revolutionary diagnostic device called the MChip, which is capable of quickly and accurately identifying many influenza viruses, including H5N1.

Tuberculosis (TB) is another emerging threat, especially with regard to new and dangerous drug-resistant forms of *Mycobacterium tuberculosis* that are being seen with increasing frequency. About one-third of the global population is latently infected with the TB bacterium. WHO estimates that 8.9 million TB cases occurred in 2004, as did 1.7 million TB deaths; active TB is especially common among people with HIV. Currently, about 20 percent of new TB cases are a multi-drug resistant form (MDR–TB), meaning that they are resistant to two common and inexpensive antibiotics and are thus far more difficult to treat than uncomplicated TB cases. However, an even more resistant form, called extensively-drug resistant TB (XDR–TB), has appeared. XDR–TB already accounts for about 10 percent of all MDR–TB cases, that is, two percent of all new TB cases.

The emergence of XDR–TB was not unexpected, but was a predictable consequence of imperfect compliance with the long and complex regimens needed to treat TB. We have long supported a large portfolio of research to develop new drugs, vaccines, and diagnostics for TB and to evaluate improved treatment and prevention regimens. As a result of that sustained effort, the "pipeline" of new countermeasures for TB is robust. At least nine new drugs are currently in clinical trials, including

SQ–109, a promising candidate being developed in a private-public partnership with Sequella, Inc. After a hiatus of 60 years in which no new TB vaccines were clinically tested, nine candidates are now in human trials, and at least ten more are in preclinical development. In addition, to ensure that the NIAID TB research program continues to contribute effectively to the global response to this increasing threat, the Institute has developed a comprehensive strategic plan for MDR/XDR–TB that will help guide our research efforts. .

Influenza and TB are just two of many emerging and re-emerging infections on which NIAID conducts research. Malaria, long a leading cause of death worldwide, has become even more problematic because of the emergence of drug-resistant malaria parasites and insecticide-resistant mosquito vectors. NIAID supports a large portfolio of malaria research that has generated many promising drug and vaccine candidates, some of which are now in clinical trials; this research is related to the President's Malaria Initiative, which was discussed at the December 2006 White House Malaria Summit. In addition, NIAID conducts research on many other less common, but nonetheless important tropical diseases such as leishmaniasis, trypanosomiasis, hookworm, and lymphatic filariasis, which exact an enormous toll worldwide.

HIV/AIDS RESEARCH

In the almost 26 years since it was first recognized, the acquired immune deficiency syndrome (AIDS) has become a global catastrophe. An estimated 39.5 million people worldwide are infected with HIV, the virus that causes AIDS. In 2006 alone, an estimated 4.3 million people were newly infected with HIV, and 2.9 million died of AIDS.

Although the global HIV situation remains grim, our government's investment in HIV research has generated many solid successes, and the healthy pipeline of new drugs, vaccines, and other prevention methods promises more successes in the future. Antiretroviral therapies made possible by NIAID-supported research have transformed HIV from an almost uniformly fatal infection into a manageable chronic condition. In this regard, a recent study concluded that since 1996 these antiretroviral medications have saved at least 3 million years of life in the United States alone. These life-saving therapies are now reaching the developing world: 1.6 million persons are now receiving antiretroviral therapy, more than half of them with support from the President's Emergency Plan for AIDS Relief (PEPFAR). In addition to these accomplishments, several new generation antiviral drugs that target HIV in novel ways are in the final stages of development.

Prevention efforts continue to be a major component of NIAID's HIV research program. We have improved our ability to prevent mother-to-child transmission. Research to develop topical microbicides capable of blocking HIV transmission during sexual contact is proceeding vigorously. And in December 2006, two NIAID-supported trials in Kenya and Uganda showed that medically supervised circumcision of adult males can significantly lower their risk of contracting HIV through heterosexual intercourse. The most powerful tool to prevent HIV infection would be a safe and effective HIV vaccine. NIAID is currently supporting 20 clinical trials of HIV vaccine candidates. Seven of these have moved beyond initial Phase I safety and immunogenicity testing. For example, in January 2007, a Phase IIb "proof of concept" trial of a non-replicating adenovirus vector modified to contain three HIV genes opened in South Africa. A related trial of the same candidate is ongoing in volunteers from North America, South America, Australia, and the Caribbean in collaboration with Merck pharmaceutical company. The NIAID Vaccine Research Center has also developed an HIV vaccine candidate that is currently being tested in Phase II trials, with an international Phase IIb efficacy trial set to begin later in 2007. Because of the enormous need for human testing of HIV drug, vaccine, and other prevention strategies, we recently reorganized our HIV/AIDS clinical trials network to make our clinical research capacity more efficient so that we can continue to meet evolving global AIDS research challenges. Additionally, NIH will contribute $300 million to the Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria in fiscal year 2008.

BIODEFENSE RESEARCH

The possibility that terrorists will use a biological agent to mount an attack is a serious threat to the citizens of our nation and the world. Research to preempt and mitigate this threat is a key focus of NIAID, and complements our role in meeting the challenges of naturally emerging and re-emerging infectious diseases. Our strategic planning for biodefense research includes three essential pillars: infrastructure needed to safely conduct research on dangerous pathogens; basic research

on microbes and host immune defenses that serves as the foundation for applied research; and targeted, milestone-driven development of medical countermeasures to create the vaccines, therapeutics and diagnostics that we would need in the event of a bioterror attack. These efforts enhance not only our preparedness for a bioterrorism attack, but for naturally occurring endemic and emerging infectious diseases as well.

NIAID has undertaken a substantial expansion of biocontainment research facilities, which will greatly enhance our ability to safely and efficiently conduct research on infectious agents. For example, through its extramural program, NIAID is supporting the construction of two National Biocontainment Laboratories capable of safely containing the most deadly pathogens, as well as thirteen Regional Biocontainment Laboratories nationwide. Three intramural biocontainment labs—on the NIH campus, on the National Interagency Biodefense Campus at Fort Detrick in Fredrick, Maryland, and at the NIAID Rocky Mountain Laboratories in Hamilton, Montana—are either complete or well under construction. In addition to these facilities, NIAID has established a nationwide network of ten Regional Centers of Excellence (RCEs) for Biodefense and Emerging Infectious Diseases Research, which conduct research and development activities and provide training for future biodefense researchers.

The Institute's efforts have already yielded substantial dividends as described in our periodic progress reports, the latest of which was issued in January 2007. For example, new or improved vaccines and therapies against anthrax, smallpox and Ebola virus have shown great promise; among these is ST–246, a promising smallpox drug candidate that protects both rodents and nonhuman primates from lethal challenge.

NIAID also has been assigned the responsibility to coordinate research to develop countermeasures against a range of radiological and chemical threats. We have established eight Centers for Medical Countermeasures against Radiation and four Centers for Countermeasures against Chemical Threats; in addition, basic and applied research is moving rapidly. We continue to coordinate and collaborate on these important components of our national security with our sister Institutes at NIH as well as interagency partners, including the Department of Defense, Department of Energy, and Department of Homeland Security.

RESEARCH ON IMMUNE-MEDIATED DISEASES

Autoimmune diseases, allergic diseases, asthma and other immune-mediated diseases are significant causes of chronic disease and disability in the United States and throughout the world. NIAID-supported research in immune-mediated diseases has led to significant advances in our understanding of how to manage these diseases.

One promising strategy to treat and prevent immune-mediated diseases is the induction of immune tolerance. Immune tolerance therapies are designed to "reprogram" immune cells to eliminate injurious immune responses, such as those seen in autoimmune diseases, while preserving protective responses needed to fight infection. NIAID has established a comprehensive program in immune tolerance research, including basic research, preclinical testing of promising strategies in nonhuman primates, and clinical evaluation through the Immune Tolerance Network (ITN). In an important study of people with severe diabetes, the ITN has shown that the transplantation of pancreatic cells can improve blood sugar control, protect patients from severely low blood sugar, and, in a few cases, relieve patients of the need for insulin injections; unfortunately, insulin independence was not sustained in most subjects. Further research is underway to improve this promising procedure.

Last year, NIAID-supported scientists reported the identification of new ways to non-invasively assess the risk of kidney graft rejection by using gene-expression based biomarkers of immunologic activity present in urine. These investigators are now conducting a multi-center study to validate these approaches that potentially could allow physicians to predict, prevent, and treat kidney rejection more effectively.

NIAID remains committed to improving the health of children with asthma, particularly those who live in our Nation's inner cities. The NIAID-supported Inner City Asthma Consortium (ICAC) has undertaken two important efforts in this area. The ICAC is conducting the Urban Environment and Childhood Asthma (URECA) Study. Five hundred and fifty inner-city children have been enrolled at birth and will be followed prospectively during childhood. The goals of the study are to identify the immunologic causes of the development of recurrent wheezing, a surrogate

marker for asthma in children under three, and to monitor the development of food allergies in this patient population.

CONCLUSION

The research conducted at NIAID and at NIAID-sponsored laboratories encompasses a broad array of basic, applied and clinical studies. This research has resulted in tangible benefits to the American public and to individuals throughout the world. By supporting talented researchers and emphasizing a balance of basic studies and targeted research, we will continue to develop innovative interventions to prevent, diagnose, and treat the wide range of infectious and immune-mediated diseases that afflict humanity.

COORDINATION WITH CDC

Senator HARKIN. Would it be safe to say, Dr. Fauci that your Institute probably intersects with CDC more than any other Institute?

Dr. FAUCI. I would think that would be safe to say. Several of the other Institutes do interact with CDC. But since CDC is responsible for the disease surveillance of those precise diseases, those emerging infections, that we are responsible for the research that develop the counter measures. There's a natural marriage between our Institutions in working together.

COORDINATION WITH DEPARTMENT OF DEFENSE

Senator STEVENS. Dr. Fauci, we've put up a lot of money through the defense bill for similar endeavors. Do you coordinate with them?

Dr. FAUCI. Indeed we do, Senator Stevens. In fact, we have very robust collaborations with them. A couple of examples have been influenza, the bio-defense, the HIV and malaria as just four examples of things that we work very, very closely with the Department of Defense.

In fact, we have cooperative agreements with them. In our biodefense area we actually have a facility that's with them up at Fort Detrick. So the Department of Defense, NIH, NIAID interaction is very, very healthy.

Senator STEVENS. So there's not a redundancy there. You are keeping that coordinated, so it's not going to be.

Dr. FAUCI. It's complementary as opposed to redundant.

Senator STEVENS. Thank you.

Senator HARKIN. Now we turn to Dr. John Niederhuber, who became Director of the National Cancer Institute in September 2006. Also served as NCI's acting Director and Deputy Director. He received his MD from the Ohio State University School of Medicine and his research at the NCI has focused on the study of tissue stem cells as the cell of origin for cancer. Interesting.

Dr. Niederhuber, thank you very much for being here. You may proceed.

STATEMENT OF DR. JOHN E. NIEDERHUBER, DIRECTOR, NATIONAL CANCER INSTITUTE, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Dr. NIEDERHUBER. Chairman Harkin, Senator Stevens and members of the staff, thank you for the opportunity to testify today on behalf of the National Cancer Institute and the National Institutes of Health.

Over the next few minutes, I would like to describe some of the progress NCI has made in cancer research along with some of the exciting opportunities we are pursuing.

For 2 years now we have seen unprecedented decreases in the actual number of cancer deaths nationally. That is remarkable news considering cancer is largely a disease of aging and as you know our country is not only growing older, its population is also growing.

Today's progress is occurring in no small part because researchers are coming to understand cancer's basic biologic processes. The sequencing of a human genome, a singular landmark in biomedical research, is providing a foundation for NCI's new Center of Human Cancer Genomics. Its mission is to systematically identify all important inherited and acquired genetic alterations that now contribute to a person's cancer risk and if cancer occurs, that cancer will behave. We are diligently working to understand these genetic changes and apply them to cancer prevention and to cancer treatment.

Consider if you will that under the microscope, diffused, large B-cell lymphoma tumors from different patients look the same. However, when subjected to gene expression analysis, they have distinct genetic signatures. These differences in their genetic signature predict prognosis and enable us to individually characterize a patient's cancer and match him or her with the best treatment. Importantly, this is not a futuristic technique. We are already beginning to apply this technology in clinical settings such as lymphoma, lung and breast cancer.

At the same time we are learning more about the mechanisms of a cancer cell including a small subset of cells within the tumor that drive the steps of invasion and growth. This subset of cells may enable the tumor to spread. Interestingly, these cells have stem cell like characteristics.

Evidence is building that these so called cancer initiators, or transformed tissue stem cells are the driving force behind many tumors, and are the basis for long term risk of cancer recurrence. Clearly these cells will be a necessary target for treatment of the future.

As we move toward an era of personalized medicine, advanced technologies will play a significant role in cancer prevention and preemption telling us in real time if a new drug treatment is reaching its target within the cell, if the novel drug is saturating that target, or if it is changing the function of the target. These early phase tests in patients will make go or no go decisions possible within hours, not within months for early cancer drug development, thus shortening development time and greatly decreasing cost.

We also realize, however, that most cancer patients have yet to see the benefits of our science. Too many patients lack the means, the mobility or even the language capacity to travel to a premier facility. It is clear that access to care will be one of the greatest determinants of cancer mortality in the years ahead.

Mindful of our mission to conduct research in all areas of science, including the behavioral sciences, such as how best to provide patient education and access to optimal care, NCI will in the next few

weeks launch the pilot phase of a community cancer centers program that if fully implemented will bring state of the art cancer care to patients in community hospitals across the United States. This program will encourage and foster the collaboration of private practice medical, surgical and radiation oncologists with the opportunity for close links to NCI's research and to our NCI designated cancer centers.

PREPARED STATEMENT

There is great cause for optimism in cancer science. But it must be tempered by an understanding of the hurdles we face. Cancer is a disease of staggering complexity with a singular name. Our progress is exciting. It is certainly encouraging, but we are continually challenged—challenged by our fellow citizens living with cancer to make faster progress.

Thank you for the opportunity to testify before the Subcommittee this afternoon.

[The statement follows:]

PREPARED STATEMENT OF DR. JOHN E. NIEDERHUBER

INTRODUCTION

I am most pleased to be before you today to report on the Nation's progress in cancer research. While there has been a steady decline in the cancer mortality rate (the number of cancer deaths per 100,000 people) since 1991, we now have the excellent news that—for the second year in a row—there has been a decline in the absolute number of cancer deaths. In 2003, there were 369 fewer cancer deaths reported in the United States than in 2002. In 2004 (the most recent year reported) the decrease was almost ten times greater, at 3,014 [Figure 1]. This decline is even more significant when you consider that cancer is largely a disease of aging, and our population is not only growing in numbers, it is aging at an even greater rate. Progress is, indeed, heartening, but our work is not done. Too many of our citizens—patients and families alike—continue to feel the pain and fear that come with the devastating news of a cancer diagnosis.

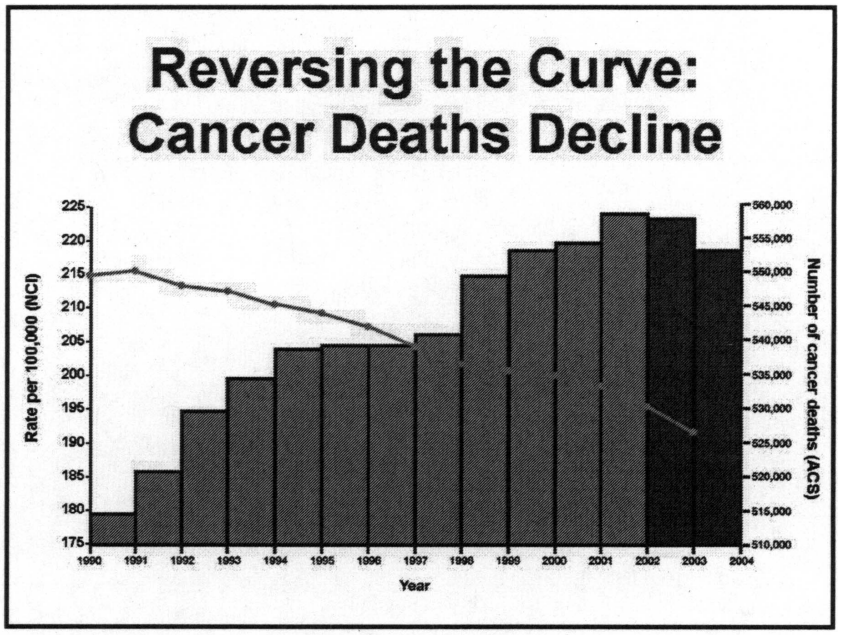


FIGURE 1.—*The green line represents the cancer mortality rate per 100,000 population. The bars represent the actual recorded number of cancer deaths in the United States.*

While we measure our progress against cancer in terms of patients treated and lives saved, that effort also has a measurable economic impact. It has been projected that even a 1 percent decrease in cancer mortality will result in a $500 billion benefit to the U.S. economy (Murphy, K. and Topel, R., Journal of Political Economy, 2006; 114(5), 871–904). In fact, such a benefit may ultimately be magnified many fold, because increasingly we recognize that cancer has become a model for developing our base of knowledge concerning many diseases. For example, the study of angiogenesis (blood vessel development) associated with tumor growth has been applied to greater understandings and treatment of macular degeneration, ischemic heart disease, diabetic wound healing, endometriosis and neurodegenerative illnesses. Furthermore, the unique capabilities of NCI's cancer researchers have been vital in other conditions. The identification of the AIDS virus and the development of assays to screen banked blood for the AIDS virus happened at the National Cancer Institute, where the current AIDS therapy regimen used around the world was also developed.

Today, the NCI is leading the way in identifying the genetic, molecular, and cellular mechanisms associated with cancer—research fronts that hold great potential to enhance research and research collaboration against other diseases, as well. Building upon the sequencing of the human genome and working in our newly developed "Center for Human Cancer Genomics," NCI is systematically identifying all the important inherited and acquired genetic alterations that contribute to cancer susceptibility. We are cataloguing genetic changes involved in the process of a normal cell becoming malignant, and we are applying this knowledge, in order to identify people at increased risk for developing cancer, prevent and detect cancer at its earliest, most treatable stages, and identify new targets for highly selective and specific therapeutic agents.

A RECORD OF REAL SUCCESS

The past year for cancer research and development has been one of substantial and heartening achievement. We are expanding both our knowledge and the technology tools to understand the mechanisms of cancer. Importantly, we are seeing scientific advances being rapidly applied to predict and preempt cancer.

—We reached an important public health milestone in June 2006, when the FDA approved a vaccine that prevents infection by the two types of the human papillomavirus (HPV) responsible for up to 70 percent of cervical cancer cases worldwide. We can all take great pride in the fact that our Nation's strong commitment to and investment in cancer research at NCI led to this approval.

—Researchers have begun to survey the human genome for DNA variants, to identify genes that predict risk for common cancers. Capitalizing on new knowledge of human genetic variation and technical advances in whole-genome scanning, The Cancer Genetic Markers of Susceptibility (CGEMS) project is currently targeting genes that increase the risk of prostate and breast cancer [Figure 2]. Work is beginning on a similar study for pancreatic cancer. These studies of large numbers of patients will be useful both for understanding causal pathways and for developing preventive interventions. DNA variants found to be associated with cancer risk will rapidly be made available publicly to the scientific community through the NCI cancer Biomedical Informatics Grid (caBIG?) database.

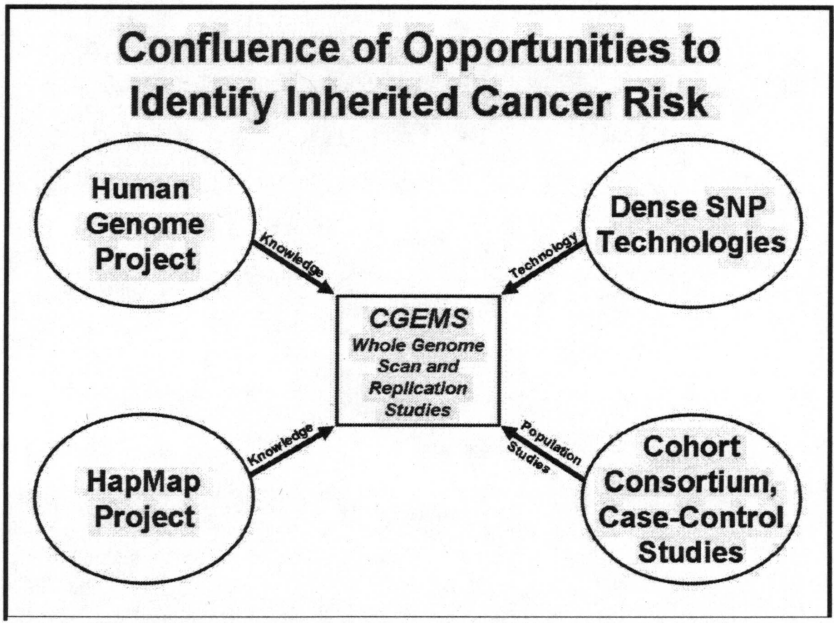


FIGURE 2.—*Previously developed technologies are used to analyze DNA specimens from large patient cohorts.*

—Genomic technology is already being applied to explain why some patients with diffuse large B-cell lymphomas (DLBCL) live longer and respond better to therapy than others [Figure 3]. Under the microscope, the DLBCL cancer cells from every patient look the same, but genetic differences have been shown to predict good versus poor prognosis. As a result of this research, it may be possible to determine which patients are most likely to respond to a specific treatment, thus sparing those patients unlikely to see a significant benefit the side effects of a failed treatment.

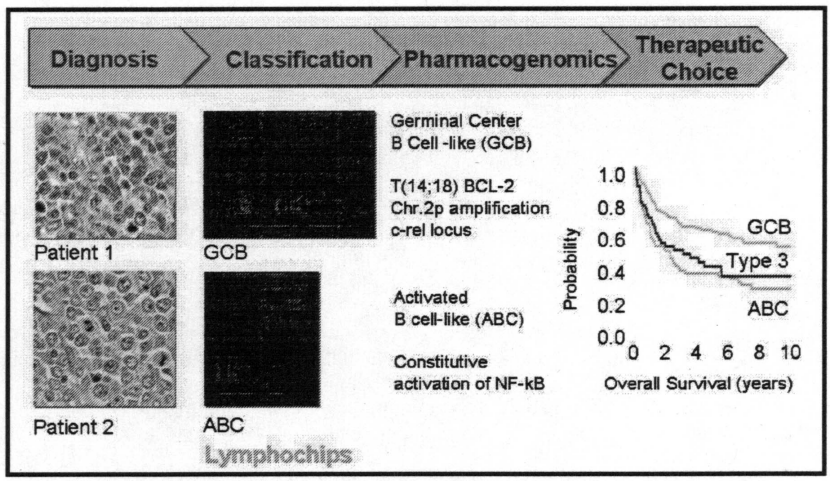


FIGURE 3.—*Previously developed technologies are used to analyze DNA specimens from large patient cohorts.*

DELVING DEEPLY INTO THE CANCER CELL ENVIRONMENT

Building on the success of the CGEMS project in identifying inherited genetic risks, the NCI and the National Human Genome Research Institute have launched a pilot phase of The Cancer Genome Atlas (TCGA), a collaboration designed to determine the feasibility of using large-scale genome analysis technology to identify important genetic changes involved in cancer. TCGA is currently studying lung, brain (glioblastoma), and ovarian cancers—which collectively account for more than 210,000 cancer cases each year in the United States.

Other initiatives are expanding our study of the cancer cell—and the networks and the cellular microenvironment that also appear to be significantly involved in tumor development and metastasis. These studies of molecular carcinogenesis are being conducted at the single-cell or the subcellular level, using high-resolution, three-dimensional electron microscopy. These technologies allow us to look within the nucleus to study differences in chromosome movement and location during stages of abnormal cell growth.

On another front, there is increasing evidence that cancer "stem cells" or "cancer initiator" cells are both the driving force behind many cancers and the basis for long-term risk. The presence of such cells, first demonstrated in acute myeloid leukemia patients, provides a different and exciting model with which to further explore cancer biology. NCI is establishing a group of scientists across the National Institutes of Health interested in embryogenesis and cancer stem cell biology, in order to advance the study of the underlying mechanisms in these processes.

ADVANCED TECHNOLOGIES ACCELERATE PROGRESS

It is clear that the area of advanced technologies development is absolutely essential and critical in creating tools for speeding up and enabling the discovery process. In addition to the genomic technology projects (CGEMS and TCGA), NCI is investing in the development of critical technology platforms in a number of other strategic areas, such as nanobiology, proteomics and computational biology.

Recognizing the key role of biospecimens in all of biomedical research, not just cancer research, NCI has led a pioneering effort to provide the first guidelines that standardize and enhance specimen collection and biorepositories. These guidelines have made it possible for NCI to develop a common biorepository infrastructure that promotes resource-sharing and enables data comparison among research laboratories, while also ensuring patient protection and ethical integrity.

We also believe that advanced imaging technologies will play a significant role in the prevention and preemption of cancer, as well as in making "go or no-go" decisions for early oncologic drug development. The NCI is working now in the aforementioned subcellular space, to be able to view—in real time—the interactions between drugs and cells and the resulting secondary functional changes. The NCI is

developing new targeted and non-targeted molecular imaging agents for use as lymphatic markers, angiogenic markers, and surrogate markers for drugs that enhance quantitative methods to measure early, real-time tumor response. These technologies are further examples of NCI initiatives that produce benefits that will be realized across multiple areas of biomedical research.

INTERAGENCY COLLABORATIONS

Addressing cancer requires work across institutional and sector boundaries, so members of the Department of Health and Human Services (DHHS) family of agencies, other federal offices, and the private sector can share knowledge and partner in the development of systems-based solutions. NCI has long been at the forefront of research and development of biomarkers for use in diagnosis and treatment for cancer. Now, a Biomarkers Consortium launched last year includes participants from the Foundation for the NIH, NIH, FDA, CMS, and private industry—with the goal of validating biological markers for a variety of diseases, including cancer. The first project approved by the Consortium is the evaluation of an imaging agent that detects an increase in cell metabolism characteristic of tumor growth. NCI is conducting trials in lung cancer and non-Hodgkin's lymphoma that use this ability to view cellular metabolism to monitor tumor masses for increased activity (cell growth) or decreased activity (cell death) during the early stages of anticancer treatment.

The joint NCI–FDA Interagency Oncology Task Force (IOTF), established in 2003 to enhance and accelerate the overall process of developing new cancer interventions, released two new guidance documents and a final rule intended to streamline the early clinical development of new drugs and biologics for cancer and other diseases. This has enabled the first-in-human "Phase 0" trial (a step before the classic Phase 1 level of drug study) that measures the activity of a new drug in a limited number of patients using a single, small dose of the study agent, prior to the traditional dose-escalation, safety and tolerance studies. Phase 0 will substantially compress drug development time.

TRAINING THE NEXT GENERATION OF CANCER RESEARCHERS

Cancer is one of the most exciting and innovative areas of medical research. It takes a superbly trained, highly effective workforce to make discoveries, to translate them into new interventions, and to put the improved knowledge base and cutting-edge tools to work for patients. NCI will continue to play an important role in developing the cancer research workforce in the United States and in other countries. We stand firmly by the Institute's commitment to provide unparalleled training opportunities for talented researchers from a wide variety of disciplines to advance their careers. In fact, many of the current programs at NIH had their origins in the NCI.

Of special significance are minority training programs, such as the Continuing Umbrella of Research Experiences (CURE), which begins with talented minority high-school students and continues progressively and selectively through long-term funding to qualified minority students interested in scientific, cancer research-related careers.

REACHING THE PATIENT AND COMMUNITY

NCI must continue to make progress for each cancer patient. Yet, the recent report on cancer deaths that showed a decrease in deaths nationally also confirms a troubling fact: Minority and low-income populations shoulder a disproportionate cancer burden and are not benefiting equally from important advances. We must bring the best science to patients, 85 percent of whom are treated in the communities where they live. With that obligation in mind, NCI is launching a pilot of the Community Cancer Centers Program (NCCCP). This pilot project will study how best to provide easily accessible, state-of-the-art, multi-specialty cancer care and earliest phase clinical trials research to patients in their communities. Through this program we will also learn best how to educate patients concerning risk, healthier living, screening practices, clinical trial participation, survivorship, and end-of-life issues.

This program is about bringing the newest science to patients where they live—a challenge that is more critical now than at any time in our history. Our nation's healthcare system faces many looming stresses, particularly in light of the fact that the first wave of baby boomers turns 65 in 2011. With the graying of a generation comes the need for a new way to confront the diseases of aging—and especially to anticipate what will be a marked increase in cancer incidence. That makes even more important our efforts to develop advanced technologies that will eventually

lead to the genomic and proteomic breakthroughs essential to enable us to preempt disease at earlier stages.

There is great cause for optimism, but an optimism that should be tempered by an understanding of the very real hurdles to progress we still face. These are challenges that we must address as a community. In doing so, the encouraging trends of decreasing death rates from cancer will become the rule, not the exception. We will learn how to deliver the best of our science to everyone—not just a few.

Senator HARKIN. Thank you, Dr. Niederhuber. Let's go on here unless you have a specific question right now.

Senator STEVENS. No.

Senator HARKIN. Dr. Barbara Alving was named as the Director of the National Center for Research Resources in April, although she served as acting Director before that. Her medical degree is from Georgetown University School of Medicine. Dr. Alving has published more than 100 papers in the areas of thrombosis and hemostasis.

Dr. Alving, welcome to the committee.

STATEMENT OF DR. BARBARA M. ALVING, DIRECTOR, NATIONAL CENTER FOR RESEARCH RESOURCES

Dr. ALVING. Thank you. Mr. Chairman, Senator Stevens, It's a great honor to discuss the mission and activities of the National Center for Research Resources today.

The research center is very different from the two ICs that you've heard about earlier. They are categorical. They're focused on specific disease areas, specific missions. The National Center for Research Resources, which is greater than a $1 billion center. Is really focused on providing the infrastructure and support to investigators and institutions throughout the country. That can really provide the support for studies in the categorical diseases.

CLINICAL AND TRANSLATIONAL RESEARCH

What we are focusing on at NCRR is clinical and translational research. By that, we're focusing on the ability to go from very basic studies, into preclinical studies, into clinical trials, and dissemination out into the public. The NCRR is very well situated for this.

For example, we have a division of comparative medicine that provides animal resources for the preclinical studies that are needed to test drugs before they go into clinical trials. We fund the eight national primate centers. I might add we also support Chimp Haven for the long-term retirement of those chimpanzees that have been involved in research.

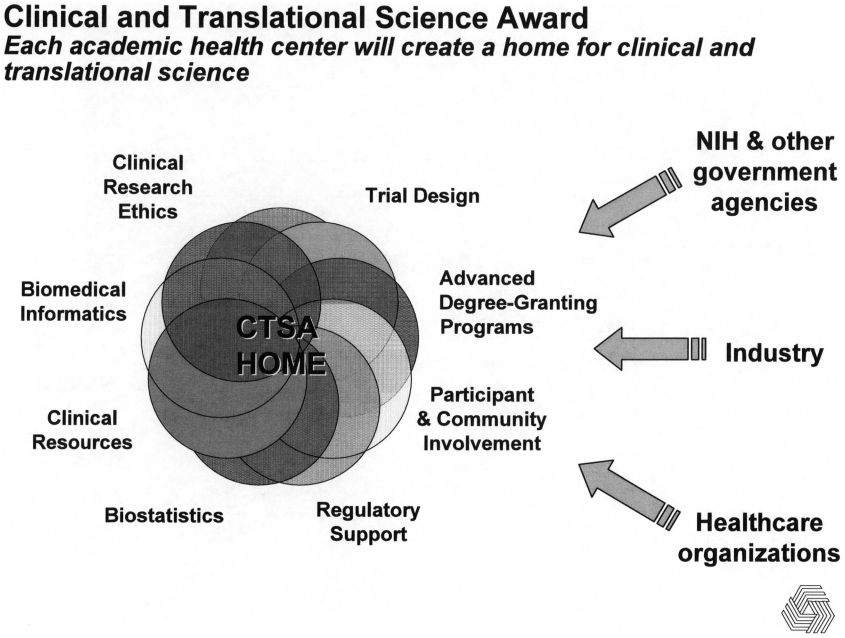
We fund biomedical technology resources that provide cutting edge research in new imaging techniques that can then be used in clinical trials.

We fund the General Clinical Research Centers that have been situated at academic institutions throughout the country to provide better ways to conduct clinical trials and the resources needed for biostatistics. What's very exciting is that this program of General Clinical Research Centers is now transitioning into a very large program known as the Clinical and Translational Science Awards.

In addition we fund outreach programs through our Science Education Partnership Awards that allow investigators to actually partner with museums to have public displays on, for example, re-

search opportunities, discussions of stem cell research, so that children throughout school systems can learn much more about the type of science, as well as the chronic diseases that are being studied in this country.

On the second slide here you see a little swirly area which represents a clinical and translational science award for an academic health center. As we have said, the General Clinical Research Centers that are funded throughout the United States are now going to be the academic health centers transitioning into receiving these clinical and translational science awards.

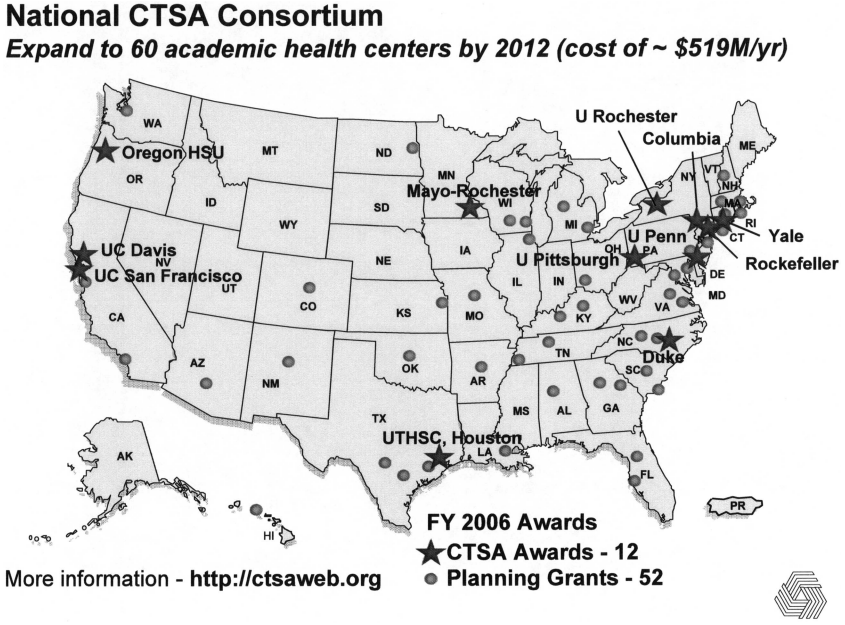


This means that each academic health center that receives such an award agrees to form a home for clinical and translational science. This will make all of our studies much more efficient, so that we can bring new research and new drugs out into the public much more rapidly and train a new generation of clinical and translational researchers. So they'll know how to interact with the FDA and they'll understand the rules. They will know how to develop better ways of doing clinical trials so that we can have more rapid accrual and less time delay and less expense.

Each of these academic health centers has agreed to form partnerships with the others, so this is really a consortium, and they will interact with industry as well as with other organizations such as Kaiser Permanente and the VA. These organizations are very rich in informatics and we want to bring interoperable informatics information systems throughout the country.

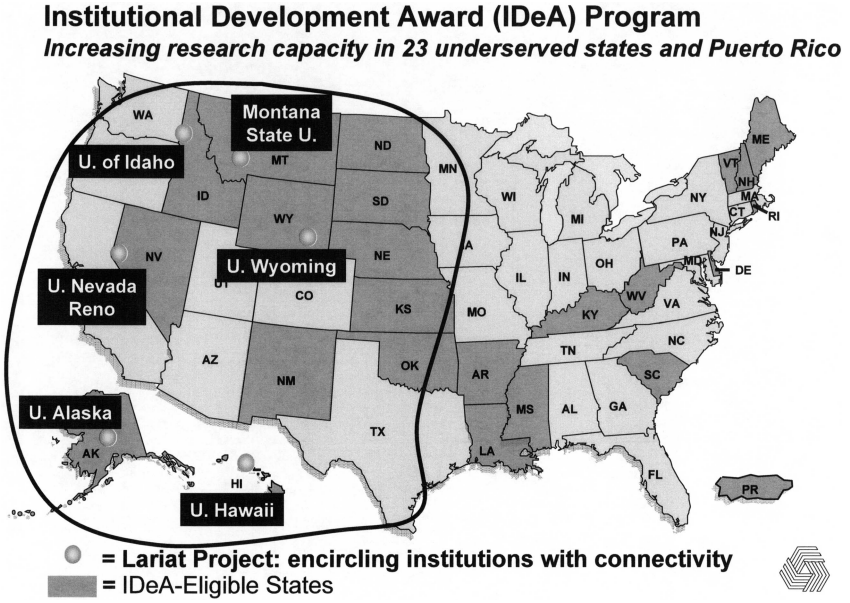
The third slide shows the United States in yellow. The little red stars show the first 12 CTSAs that have been awarded throughout the country. This was done in October 2006, along with 52 planning grants. By 2012, we hope to have 60 CTSA awards at a total

annual cost of $500 million per year. But we fund other large programs at NCRR, and we want to create a matrix of interactions with programs.



INSTITUTIONAL DEVELOPMENT AWARD

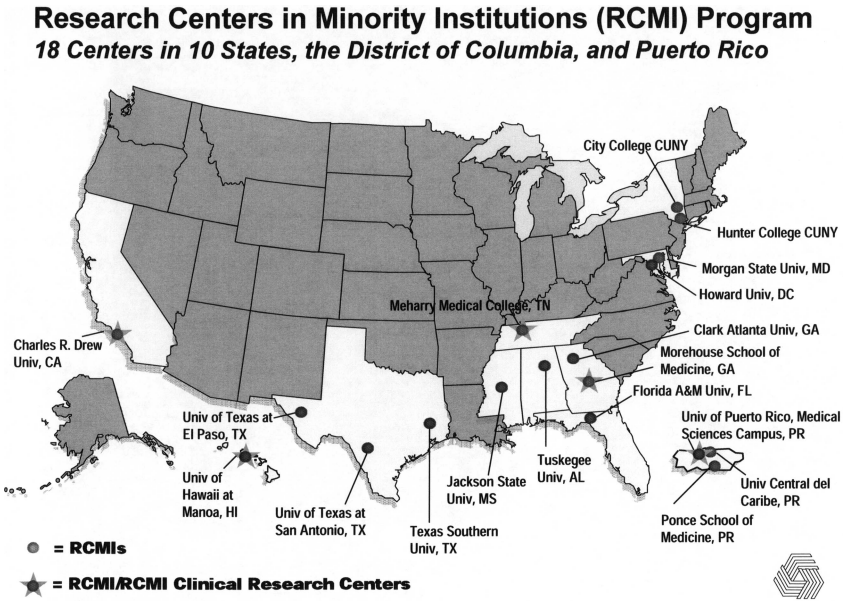
In the fourth slide you see the IDeA program. I think Senator Stevens is probably very well aware of this program. It is providing funding to 23 States and Puerto Rico that receive less—historically a lower amount of NIH funding. This is usually due because they have rural populations or small populations. These awards are allowing students from undergraduate colleges to have access to research training in some of the larger universities in these States.



We also realize they need to be connected because of their vast challenges of distance. So you see in the slide that shows the green States, those are the IDeA States red line which is Lariat. That's really a lasso to bring high speed information systems and fiber optic networks to six States that are very, very far apart that need to be connected. So through this Lariat project we've connected Hawaii, Alaska, Idaho, Nevada, Montana, and Wyoming. This provides the latest opportunities to conduct science through this high speed fiber optic system. It also has improved the economies of these States and allows the delivery of health care. We want to continue this in other areas.

RESEARCH CENTERS IN MINORITY INSTITUTIONS

If you go to the fifth slide to the map of the United States, you see another picture. You see the Research Centers in Minority Institutions. These are centers that include historically black academic health centers and Hispanic centers. These too, need to be linked up and have the latest opportunities.



We provide funding to these centers to conduct clinical research and training as well as basic research. What we're doing now is encouraging them and they are very eager to link up into this new clinical and translational science program. So we have Meharry talking with Vanderbilt. Morehouse is talking with Emory. Charles Drew is talking with UCLA. How can they form partnerships? How can they provide outreach to the communities?

MATRIX OF OPPORTUNITIES

Basically, at NCRR, we are now focusing throughout the center on translational and clinical sciences. We want to create a matrix of opportunities for this nationally, geographically and racially diverse matrix of academic health centers and other institutions. We want to include links to PHARMA, biotech, state and Federal agencies, as well as to CMS and the FDA, so that we can have a seamless interaction.

PREPARED STATEMENT

The whole result of this will be to provide better access to health care to our diverse populations. We're very aware of the increased amount of money going to health care. We want to make this much more efficient. We want to train the new generations of investigators who have to carry out this work.

Thank you for the opportunity to discuss this.

[The statement follows:]

PREPARED STATEMENT OF HON. BARBARA M. ALVING

Mr. Chairman and Members of the Committee: It is a privilege to present to you the President's budget request for the National Center for Research Resources (NCRR) for fiscal year 2008. The fiscal year 2008 budget includes $1,112,498,000. I appreciate this opportunity to discuss with you our vision of the future of health

and medicine and to share ways NCRR programs are transforming clinical and translational research.

The NCRR, which is one of the 27 Institutes and Centers at the National Institutes of Health (NIH), provides NIH-supported laboratory and clinical researchers with the infrastructure, tools, and training they need to understand, detect, treat, and prevent a wide range of diseases. With this support, scientists engage in basic laboratory research, translate these findings to animal-based studies, and then apply them to patient-oriented research. Through innovative programs and resources that transcend geographical boundaries, NCRR connects researchers with one another, and with patients and communities across the Nation. These connections bring together innovative research teams and the power of shared resources, multiplying the opportunities to improve human health.

TRANSFORMING CLINICAL RESEARCH

Given its mission and support to more than 30,000 basic and clinical researchers, NCRR has become the leader of the NIH Roadmap for Medical Research effort to energize the discipline of clinical and translational research. To remove the barriers identified by the research community, NCRR launched the Clinical and Translational Science Award (CTSA) program, which is a national consortium designed to more rapidly and efficiently facilitate the transfer of discoveries made in the laboratory into new treatments for patients. Through the CTSAs, academic health centers are developing centers, departments, or institutions for interdisciplinary teams that cover the complete spectrum of research from basic biology to clinical medicine. These academic homes also will train the next generation of researchers in translational and clinical research.

On September 30, 2006, we made the first CTSA awards to 12 academic health centers throughout the country. We will award the second group of CTSAs this fall. By 2012, the CTSA Consortium is expected to include approximately 60 CTSAs.

The impact of the CTSA Consortium will be far greater than the number of awards made. The Consortium will develop better designs for clinical trials, forge new partnerships with health care organizations, and expand outreach to minority and medically underserved communities. The CTSAs will focus on both types of translational research—ensuring first that basic discoveries are applied to the clinic and second that they are further translated into community practice. Improving clinical research informatics will be a prominent focus of the Consortium. Institutions are taking steps to prioritize their efforts to ensure that standards are developed, interoperability is enhanced, and communication resources are accessible to researchers and their patients.

To improve communication with the public and our stakeholders about our progress, as well as to foster collaborations within and beyond the Consortium, we recently launched the CTSAWeb.org site. I encourage you to visit the site and learn more about the CTSA Consortium. We also have started plans to evaluate the Consortium to ensure that the program spurs innovation, integration, inclusion, and dissemination.

Already, we are starting to see significant changes within and across the CTSA institutions. As a result of this effort, academic health centers are developing new curriculums, revamping their organizational structures, creating unprecedented partnerships with other medical and research disciplines, and generating medical advances. For example, the Institute for Translational Medicine and Therapeutics (ITMAT) at the University of Pennsylvania—a trans-institutional endeavor with the Children's Hospital of Philadelphia, the Wistar Institute, and the University of Sciences in Philadelphia—is leading clinical and translational research and fostering interdisciplinary science. Now with the CTSA award, ITMAT will also become the home to new centers in bioinformatics, personalized medicine, imaging, and chemical biology. At the same time, the University of Texas Health Science Center at Houston CTSA is encouraging participatory research by connecting with Hispanic communities on the border. By linking with NCRR's Science Education Partnership Award program in Houston, this CTSA is improving the public's understanding of the importance of clinical trial participation. As the CTSAs begin to work together, the benefits of the program will extend to the greater research community and ultimately be incorporated into clinical care.

I am pleased to report that this transformation is creating new energy and opportunities within NCRR and across the NIH. The CTSA initiative is further enhancing NCRR's long-standing investments in advancing translational research and providing new opportunities for community engagement. The addition of the CTSA Consortium to the matrix of NCRR programs is providing opportunities for increased cohesion and interaction throughout our entire research portfolio. Similarly,

the truly trans-NIH nature of the CTSA program is facilitating interactions among the NIH Institutes and Centers and helping to ensure that the benefits of the Consortium are realized across the full spectrum of medical research.

ADVANCING TRANSLATIONAL RESEARCH

Helping to propel the CTSA discovery engines are NCRR's translational research programs. Our readily available animal models and biomedical technology resources are fueling advancements in clinical care. We are exploring opportunities to enhance interactions among our translational programs and the CTSA Consortium to further capitalize on our research investments.

Animal models are the bridge between basic science and human medicine. The NCRR provides such models through specialized laboratory animals, research facilities, and training. Linking NCRR's animal resources with CTSAs will allow for more seamless translation from pre-clinical findings to clinical trials. This is already underway at two CTSAs, the University of California-Davis and the Oregon Health and Science University, which are connecting with the NCRR-supported National Primate Research Centers at their institutions. To provide researchers with easier access to animal models, and thus further accelerate translational research, we sponsored a workshop in 2006 to explore approaches to develop a resource that would enable researchers to find and use animal and other biological resources more efficiently. Based on stakeholder recommendations, we are planning to fund a comprehensive electronic catalog of animal model resources in fiscal year 2008.

Technologies are critical throughout all stages of biomedical research—from basic discovery to clinical application. The NCRR support for biomedical technology (BT) resource centers provides researchers with a broad spectrum of technologies, techniques, and methods. Across the nation, researchers depend on these centers for a wide variety of clinical and translational studies. For example, researchers at the University of Illinois are developing software to help analyze the motions of viruses, so that they can better predict the virulence of these organisms. At the University of Wisconsin-Madison, another BT resource center, researchers are using advanced nuclear magnetic resonance technologies to develop faster and more cost-effective methods for studying how biological systems work and respond to drugs. In the future, technologies developed at the BT resource centers may lead to discoveries that the CTSAs can translate into improved patient care.

ENHANCING COMMUNITY ENGAGEMENT

The launch of the CTSA initiative has further enhanced our appreciation of the need to actively engage not only the researchers but also the American public. Our programs are providing opportunities for people in underserved communities to participate and shape medical research. Our innovative science education programs are inspiring children to pursue careers in biomedical research and are increasing the public's understanding of medicine. By reaching out to new collaborators and strengthening our partnerships, NCRR is facilitating connections that are sparking new discoveries and maximizing the effectiveness of the matrix of NCRR programs.

NCRR has two successful programs that are creating new research opportunities for underserved communities. First, the Research Centers in Minority Institutions (RCMI) program increases the number of minority scientists engaged in biomedical research and enhances the research capacity and infrastructure at minority colleges and universities that offer doctorate degrees in health sciences. This program increases the number of minority scientists engaged in biomedical research and facilitates studies on minority health. Second, the Institutional Development Award (IDeA) program fosters health-related research and increases the competitiveness of investigators at institutions in 23 states and Puerto Rico, which have historically low aggregate success rates for grant awards from the NIH. The IDeA program provides workforce development, research opportunities, science education, and extends high-speed connectivity to IDeA institutions to facilitate research collaborations. For example, NCRR funded the Lariat Project to provide six states (Alaska, Hawaii, Idaho, Montana, Nevada, and Wyoming) with high-speed, fiber-optic network connections. This project has improved not only research capacity in these states, but also enhanced their economic development, higher education, and healthcare opportunities. To ensure these underserved communities have access to innovative research opportunities, we are exploring ways to facilitate partnerships with these communities and the CTSAs.

One of the many ways that community engagement is improving research is through a component of the IDeA program called IDeA Networks of Biomedical Research Excellence (INBRE) program. This program enables critical connections among different research institutions and facilities, as well as between mentors and

students. For example, the Montana INBRE brought together the seven tribal colleges within the state to conduct collaborative research projects. Today, these tribal colleges, which prior to the INBRE program had not interacted on research projects, are working together to identify research areas and collaborate with other undergraduate institutions within Montana.

Community engagement is synonymous with the NCRR Science Education Partnership Award (SEPA) program. By bringing together active biomedical and clinical researchers with educators, community leaders, and other interested organizational leaders, SEPA is stimulating public interest in health issues and encouraging young people to pursue careers in medical research. SEPA grantees currently collaborate with several RCMI and IDeA institutions and are beginning to make similar connections through CTSA community engagement activities. At Jackson State University, RCMI- and IDeA-funded researchers have partnered with the Jackson Public Schools through a SEPA grant to provide mentoring and research internships for students and professional development for teachers. Another SEPA project at the University of Utah, offers over 100 online activities, podcasts, and virtual labs on topics ranging from cloning to stem cells.

Innovative partnerships are providing the cohesion needed to ensure that the matrix of NCRR programs results in a maximum return on investment for all Americans. We are expanding our outreach efforts with the pharmaceutical industry, healthcare organizations and providers, and other Federal agencies, such as the Food and Drug Administration and the National Science Foundation. These collaborative partnerships will not only enable us to make research discoveries faster, but will ensure that these discoveries are quickly translated into improved patient care.

CONCLUSION

Through our matrix of programs and partnerships, NCRR expects to fulfill its charge to transform the practice of clinical and translational research and in turn, improve the future of health and medicine. The launch of the CTSA Consortium marks an exciting time in the history of NIH and for our Nation. It further enhances NCRR's long-standing investment in basic, translational, and clinical research. Our innovative programs and partnerships are maximizing our research investment to ensure that medical advances are reaching the people who need them.

Senator HARKIN. Dr. Alving, thank you very much.

Now we turn to Dr. Patricia Grady, who has served as the Director of the National Institute of Nursing Research since 1995. She pursued her graduate education at the University of Maryland, receiving a Master's Degree from the School of Nursing and a Doctorate in Physiology from the School of Medicine. Dr. Grady's scientific focus is primarily in stroke research.

Dr. Grady, welcome back to the committee.

STATEMENT OF DR. PATRICIA A. GRADY, DIRECTOR, NATIONAL INSTITUTE OF NURSING RESEARCH

Dr. GRADY. Thank you, Mr. Chairman. I appreciate the opportunity to present to you, Senator Stevens and the staff, a brief description of some of the activities that are going on at the National Institute of Nursing Research.

The NINR supports clinical and basic research to establish a scientific basis for the care of individuals across the life span. NINR's research has contributed to improving the health of the American people for more than two decades. Our 20th anniversary provided an opportunity to look toward the future and update our strategic plan which formulates innovative ways to address the major health challenges facing our Nation, including the concurrent trends of an aging population, a growing racial and cultural diversity, an increasing reliance on technology and a rising demand for nurses.

In response to these and other challenges, you heard the Director of NIH call for a new kind of health care system. In the spirit of today's hearing I would like to briefly describe for you important

research that is preemptive and predictive and how that research is shaping our vision for the future.

The first preemptive example could have major implications for improving the lives of premature infants and their parents. Current practice during the birth of a pre-term infant is to clamp the umbilical cord immediately after delivery. However, delayed cord clamping has been shown to have certain advantages for the infant.

In a recent study, NINR supported investigators compared the effect of immediate verses delayed umbilical cord clamping. The results of this simple modification were very encouraging. Infants in the delayed cord clamping group had nearly a ten-fold lower rate of late onset infection and nearly a three-fold lower rate of brain hemorrhage. Each of these complications carries a high risk of disease, disability and death.

Another study tested the effect of a coping intervention for parents of pre-term infants, in which parents participated in a program about prematurity, infant behaviors and infant development. The effect of this program was dramatic. Parents demonstrated improved parenting behaviors and reported decreased stress levels. Moreover, the infants averaged 3.8 fewer days in the Neonatal Intensive Care Unit, which translated to a savings of roughly $5,000 per infant.

Developing preemptive strategies to reduce the risk factors for cardiovascular disease is another important research focus for us. A group of investigators tested a community based behavioral educational intervention to improve blood pressure management among young African American men. The intervention reduced blood pressure and subsequently reduced by half the incidence of left ventricular hypertrophy, a form of heart damage caused by high blood pressure.

We've also made strides in studying and preventing medical errors that continue to trouble our hospitals and clinics. For example, surgical sponges accidentally left inside patients can lead to complications ranging from infection to death. NINR investigators demonstrated that a radio frequency identification tag system for surgical sponges could quickly and accurately detect the presence of sponges retained at surgery. This is just one example of the type of innovative research needed to reduce the adverse health effects and significant cost implications associated with medical errors.

Investigators have also demonstrated a clear link between low nurse staffing levels and an increase risk to patients.

Senator HARKIN. What?

Dr. GRADY. Low nurse staffing levels and an increased risk to patients. Decreased nurse staffing levels are associated with increased mortality and morbidity, specifically, infections and other complications. These studies highlight the importance of the growing national nursing shortage upon the health of our population.

Finally, nowhere is the need for better preventive and preemptive efforts greater than in the minority communities and in other underserved populations. Recently scientists reported the first randomized controlled trial of a culturally tailored HIV risk-reduction program for Hispanic adolescents, a program that was successful in reducing risky behaviors for up to 1 year.

Another group of scientists developed an intervention that reduced stress and depression in low income single mothers, improving their ability to care for their children. Programs such as these are critical for reducing health problems in vulnerable communities and demonstrate the progress we have made already.

Let me now provide you with a few examples of new methods for predicting the needs of patients and for anticipating ways to proactively maintain quality of life for patients and their caregivers. One example of predictive illness management comes from NINR's research on the care of patients at the end of life. As you probably know, NINR is the lead institute at NIH for this important area of research.

One of our research teams characterized the functional decline in patients with specific illnesses in the last year of life. Trajectories range from—sudden, unexpected death to variations in illness and recovery, to steady and irreversible decline. This knowledge helps caregivers to better anticipate the course of illness, allowing the health team to tailor treatment strategies and improve quality of care.

Yet another study showed that minority patients who used spiritual coping are more likely to want aggressive care at the end of life such as life support, tube feeding or mechanical ventilation. Such findings can allow caregivers to better incorporate the culturally based needs and desires of patients and their families.

PREPARED STATEMENT

In conclusion, NINR is strongly committed to the NIH vision of a healthier Nation. We are proud of the important progress we have made toward this goal and we look forward to continued successes. We stand ready to address tomorrow's challenges based upon our 20 years of scientific accomplishments. Thank you, Mr. Chairman, Senator Stevens. I'd be happy to answer any questions that you or the Committee might have.

[The statement follows:]

PREPARED STATEMENT OF DR. PATRICIA A. GRADY

Mr. Chairman and Members of the Committee: I appreciate the opportunity to present the fiscal year 2008 President's budget request for the National Institute of Nursing Research (NINR). The fiscal year 2008 budget included $137,800,000.

INTRODUCTION

The mission of the NINR is to support clinical and basic research that establishes a scientific basis for the care of individuals across the lifespan—from management of patients during illness and recovery to the reduction of risks for disease and disability, the promotion of healthy lifestyles, promoting quality of life in those with chronic illness, and care for individuals at the end of life. NINR's research programs also place special emphasis on eliminating health disparities and on the health issues faced by the underserved.

NINR's research has contributed to improving the health of the American people for more than two decades. In 2006, NINR concluded the year-long observance of our 20th anniversary at NIH. During that period, we took stock of our scientific accomplishments, recognized our contributions to clinical practice, and launched a newly revamped web-site in support of our stakeholders. We also assessed the future role of nursing science in addressing the major health challenges of our Nation: an aging population; a growing racial and cultural diversity and the attendant health disparities; an increasing reliance on technology in health care settings; and a rising demand for nurses. Within this context, NINR developed a new, forward-looking Strategic Plan.

NINR's new 5-year Strategic Plan elucidates a unified framework for addressing the dynamic health care landscape. The Plan leverages key strengths of the NINR research community and focuses on areas of critical research opportunity including: Self-Management, Symptom Management, and Caregiving; Health Promotion and Disease Prevention; Research Capacity Development; Technology Integration; and End-of-Life. Pursuing this strategy, we seek to apply NINR's resources to the areas of public health which have the greatest needs, and in which NINR can have the greatest impact.

Allow me to briefly describe our programs within this framework, highlight recent accomplishments, and share our vision for the future.

NINR RESEARCH PROGRAMS

Self-management, Symptom Management, and Caregiving.—NINR's focus on the quality-of-life science continuum comprises three key research concepts: self-management, symptom management, and caregiving. Self-management science explores strategies that empower individuals to be more involved in their own health practices. Symptom management science focuses on biological and behavioral components of health and illness that improve the management of symptoms. Caregiving science addresses the quality-of-life dimensions experienced by care recipients as well as formal and informal caregivers across diverse health care settings.

Improving Care of Premature Infants.—According to the Centers for Disease Control and Prevention (CDC), half a million preterm infants are born in the United States each year, carrying a significant risk of death and disability, and often requiring care in a neonatal intensive care unit (NICU). In addition, their parents endure high levels of stress, anxiety, and depression (Miles, 1999; Singer, 1999, Wereszczak, 1997).

In one study, NINR-supported investigators assessed the effect of "immediate" (7 seconds) versus "delayed" (32 seconds) umbilical cord clamping on health parameters of preterm infants. Compared to the immediate clamping group, infants in the delayed group had nearly a 10-fold lower rate of late-onset septic infection, which carries a high risk of morbidity and mortality (IOM, 2006), and nearly a 3-fold lower rate of intraventricular hemorrhage, which carries a risk of developmental deficits (IOM, 2006).

Another study by NINR-supported investigators assessed the effect of an educational program on the psychological care needs of parents of preterm infants. Utilizing the Creating Opportunities for Parental Empowerment (COPE) educational program, parents were taught about prematurity, infant behaviors, and infant development. As a result, parents demonstrated improved parenting behaviors and reported decreased stress levels. Meanwhile, the infants averaged 3.8 fewer days in the NICU than controls, which translated to a savings of roughly $5,000 per infant (Melnyk, 2006).

Taken together, these studies demonstrate the significant potential benefits of combining a minor modification to a medical procedure at virtually no cost and an educational program during the care of preterm infants to improve health outcomes while reducing health expenditures. Their adoption into standard practice, and the exploration of additional approaches, could result in a more robust reduction in prematurity-related complications in early childhood, disability, death, and health care costs in excess of the $2.5 billion in estimated potential savings through the COPE intervention alone ($5,000 savings per infant multiplied by the estimated 500,000 preterm infants born in the United States each year).

Quality-of-life research directly impacts populations across the lifespan from the very early stages of life. In 2007, NINR plans to support research on symptom clusters in cancer and immune diseases, as well as biobehavioral research methods.

Health Promotion and Disease Prevention.—Within Health Promotion and Disease Prevention, NINR scientists explore dimensions of behavior, health in community settings, patient safety, and the biological factors useful in ensuring long-term positive health outcomes.

Culturally-tailored HIV/AIDS Intervention for Hispanic Youths.—According to the CDC, the incidence of acquired immune deficiency syndrome (AIDS) is up to three times higher among Latino adolescents than among their white counterparts (CDC, 2004). NINR-supported scientists tested a culturally-tailored HIV education program called "Cuidate! (Take Care of Yourself)" among Hispanic adolescents. Compared to controls, youths in the program were 34 percent less likely to report having had sexual intercourse in the past 3 months, 47 percent less likely to report having multiple partners across the follow-up period, and reported more consistent use of condoms. This study demonstrates the benefits of a customized, population-specific

intervention and highlights its potential to reduce health disparities if applied across a range of settings (Villaruel, 2006; Jemmott 1998).

In 2007 NINR plans to support research that incorporates an in-depth knowledge of cultural factors into HIV prevention studies among young people.

Research Capacity Development.—NINR is engaged in enhancing the research capacity of nursing science. NINR supports pre- and post-doctoral training through both individual and institutional training grants. NINR also supports Research Centers to establish and maintain hubs of research, such as the NINR Nursing Partnership Centers on Health Disparities, which bring together colleagues from research intensive institutions and minority-serving schools of nursing, with the goals of exploring health disparities research questions and training investigators from underrepresented populations.

In 2008, NINR will support academic research enhancement opportunities in minority-serving institutions.

Technology Integration.—NINR's focus on improving health care and quality of life encompasses the development, use, and adaptation of technologies. Functional technologies that assist patients and those that facilitate reporting of biological indicators of health and disease status form the framework of the technology integration program, including uses of technology for telemedicine, patient education, communication, and patient safety.

Radiofrequency Identification (RFID) and Patient Safety.—The Institute of Medicine (IOM) estimates the cost of medical errors to be over $37 billion annually; nearly half is associated with preventable errors; and, up to 98,000 deaths each year are attributable to medical errors (IOM, 1999). Currently, certain medical errors such as the retention of surgical sponges within patients after surgery persist. NINR-supported scientists have demonstrated that a radiofrequency identification (RFID)-tag system for surgical sponges accurately detected the presence of sponges retained at the surgery site after wound closure was simulated. If implemented into practice, this approach may not only contribute to the reduction of medical errors, but also decrease both the time spent in the hospital as well as heath care expenditures.

In 2008, NINR plans to support studies focused on stimulating technological strategies that improve health outcomes through the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) Programs.

End-of-Life.—The science of end-of-life explores research questions of this complex period for dying persons, family members, and both professional and informal health care providers. End-of-life scientists seek to understand not only biological aspects of dying, but also the needs of dying persons, including symptom relief, decision-making, advance directives, and palliative care. In addition, issues of culture, age, spiritual beliefs, and disease-specific considerations are included in research strategies.

Chronically Critically Ill and End-of-Life Care Preferences.—Patients who are or may become chronically critically ill may benefit from having advance directives in place should they lose the ability to communicate their preferences. NINR-supported investigators examined the frequency of documentation of advance directive choices of 1,128 patients hospitalized with a chronic critical illness. Results indicate that about two-thirds did not have an advance directive to document their care preferences, and may benefit from an educational program in end-of-life care and documenting their preferences.

CONCLUSION

NINR's dedicated investigators act on their clinical experience and insight to develop and test innovative solutions to the major health challenges facing our society. Equipped with a new Strategic Plan, we aim to sustain the pace of nursing science discoveries in the years ahead by bringing together innovation and determination within a strategic framework to improve clinical practice and patient care. With 20 years of research, NINR has garnered expertise for new opportunities to address tomorrow's challenges.Thank you, Mr. Chairman. I will be happy to answer any questions that the Committee might have.

Senator HARKIN. Thank you very much, Dr. Grady.

Now we turn to Dr. John Ruffin, who is the Director of the National Center on Minority Health and Health Disparities. He's led the effort at NIH to promote minority health and reduce health disparities for over 15 years and oversaw the development of the first Comprehensive Health Disparities Strategic Plan at NIH.

Dr. Ruffin, welcome to the committee. Please proceed.

STATEMENT OF DR. JOHN RUFFIN, DIRECTOR, NATIONAL CENTER ON MINORITY HEALTH AND HEALTH DISPARITIES

Dr. RUFFIN. Thank you, Mr. Chairman, Senator Stevens. Today I'm here to give you a brief report on the progress the National Center on Minority Health and Health Disparities and the National Institutes of Health is making to promote the improvement of health among our Nation's racial and ethnic minority population. To advance research toward eliminating health disparities among all affected populations including the medically underserved, poor and rural populations.

Senator Specter, I'm sure you will recall the hearings that you and others convened in the late 1990s on minority health and health disparities. I participated in many of those hearings which ultimately led to the creation of the NCMHD. The release of the Institute of Medicine report entitled, "Unequal Treatment", came right on the heel of the Center's creation. That report, you will recall, was a vivid depiction of the state of affairs of the health care system and health among this Nation's diverse population.

Six years ago Congress established the NCMHD and gave us the authority to be the focal point at the National Institutes of Health for Minority Health and Health Disparities research. We took that authority seriously and have established the basis to fulfill our mission. There are a number of things that we know related to minority health and health disparities and then there are some unknowns that we continue to work toward understanding.

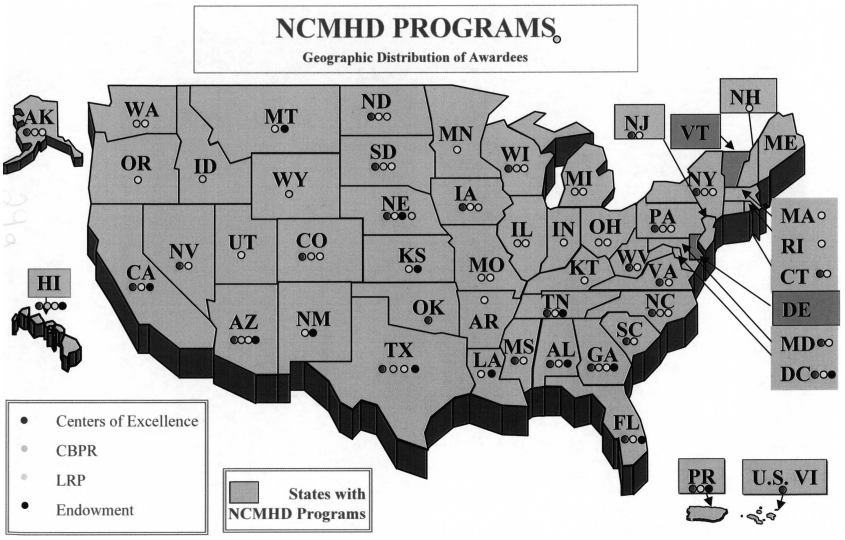
For example, what we have not yet uncovered is the cause of health disparities. We still do not know why racial and ethnic minorities and poor populations across this Nation continue to be burdened by diseases and conditions like HIV/AIDS, cancer, infant mortality, mental health and stroke, for example. What we do know is that there are multiple factors that contribute to disparities in health.

These are the types of issues that we are seeking to understand through our own research at the NCMHD as well as through the research efforts of the Institutes and Centers that my colleagues around the table spearhead, and other Institutes and Centers at NIH that are not represented here today.

Our approach to health disparities is multi-proned. Through research we study the diseases, the conditions, and the issues to gain insight into the core of the problem. To conduct research we have to have the capacity, the facilities and the workforce to carry out the studies. We also need to have the community involved, not only as research subjects, but actively engaged in planning and conducting research, translating the research results and—disseminating the information back into the communities.

To get at this, you, the Congress, statutorily mandated four initiatives that would set the framework for us to accomplish our goals in these areas. Those are our Centers of Excellence program, Research Endowment Program, Loan Repayment Program and the Community Based Participatory Research Program.

If you look at figure 1 the map, which I gave to you in the book there, you will note that geographically our programs are in every State except Vermont and Delaware. So we have set the foundation by implementing the programs that you mandated.



So what difference are we making to eliminate health disparities using this multifaceted strategy? If you look at the Centers of Excellence, much of the multidisciplinary research that we are conducting in communities across the country is being carried out through the Centers of Excellence Program that you authorized. We have funded 76 Centers nationwide since 2002.

Our research endowments have led to the establishment of educational and training facilities such as pharmacy and public health schools. We've helped approximately 17 institutions to build their competitive edge for health disparities research. In order to attract the best and the brightest to the health profession, we have made loan repayment awards to about 1,100 highly qualified doctorate level health professionals. An estimated two-thirds of the graduates have secured academic or research positions.

Imagine cutting edge biomedical research being led within our communities by members of the community. That's what our Community-Based Participatory Research Program is about. We launched this three-phase program in 2005. We received an overwhelming number of applications, approximately 180. Today we are supporting 25 grants under this program.

Mr. Chairman, our portfolio at the NCMHD is small in terms of dollars and numbers of programs, but that does not prevent us from fulfilling our mission. Collaboration is a large part of what we do within the NIH and with other agencies including my colleagues represented at this table.

Some of the initiatives within their health disparities portfolio that we have helped to support include: the Health Disparities Nursing Research Center for the National Institute of Nursing Research, the Bioethics Center at Tuskegee University with the National Center for Research Resources, research on autoimmune disease with the National Institute of Allergy and Infectious Diseases and the Vanderbilt-Meharry Comprehensive Cancer Center with the National Cancer Institute.

In conclusion, the NCMHD is making progress to predict and preempt disease through its Centers of Excellence and Community Based Participatory Research Program. We're building a culturally, competent workforce to deliver personalized medicine using the loan repayment program. Our Community-Based Participatory Research Program also embraces a critical element of medicine and that is the participatory aspect.

Overall, our contribution has heightened awareness about health disparities, has increased the Nation's capacity to conduct health disparities research, recruited, trained and attracted an increasing cadre of individuals to research careers on minority health and health disparities and germinated innovative and productive partnerships involving the community. But we have barely touched the surface. There is far more to be done.

PREPARED STATEMENT

The success of our health disparity effort, Mr. Chairman, depends upon our ability to further develop and sustain good models that we have all established. I thank you for the opportunity to brief you today.

[The statement follows:]

PREPARED STATEMENT OF DR. JOHN RUFFIN

Mr. Chairman and Members of the Committee: I am pleased to present the President's budget request for the National Center on Minority Health and Health Disparities (NCMHD) for fiscal year 2008, a sum of $194,495,000, which represents a decrease of $895,000 over the comparable fiscal year 2007 appropriation.

At the turn of the 21st century, the issue of health disparities was still a pervasive public health challenge. Racial and ethnic minority and medically underserved populations were suffering disproportionately from disease and death; individuals living in medically underserved communities in rural or urban cities were also experiencing similar disparities in health status and health outcomes; there was a national need for minority scientists in biomedical, clinical, behavioral, and health services research. There were very few racial and ethnic minorities in science, technology or engineering. This raised concern about the future of these fields and their potential to eliminate health disparities given the nation's changing demographics, and the projected significant increase of racial and ethnic minority populations.

This depiction of health in America was a part of the impetus for the creation of a national Center to address minority health and health disparities. Recognizing the gaps and the challenges, and understanding the promise of biomedical research, the Congress wisely established the National Center on Minority Health and Health Disparities (NCMHD) on the premise that through research, training, dissemination of information, and other programs, minority health would be improved, and health disparities would be reduced in the short-term and eliminated in the long-term. The NCMHD has embraced multiple partnerships as the guiding principle for understanding and addressing this national health crisis.

While the overall health of the American population has improved, sadly, health disparities have not declined. Nevertheless, within the past six years the investments of the NCMHD have positively impacted communities throughout this nation and globally. Our contributions have heightened awareness about the seriousness of health disparities; increased the nation's capacity to conduct health disparities research; recruited, trained and attracted an increasing cadre of individuals from health disparity populations to research careers on minority health and health disparities; and germinated novel and productive partnerships involving the community.

UNDERSTANDING HEALTH DISPARITIES

The Centers of Excellence program has become a leading force for research into various diseases and health conditions in health disparity populations such as HIV/AIDS, mental illness, obesity, diabetes, cardiovascular disease, stroke, infant mortality, and cancer. Collectively, these Centers have published more than 200 articles

on the priority diseases/conditions and issues related to minority health and health disparities among all racial and ethnic minority, medically underserved, and low-income populations. Leveraging of resources and expertise with other NIH Institutes and Centers and federal agencies, and among our grantees has fortified our capacity to conduct research into the most critical diseases and issues concerning disparities in health. Basic, clinical, social science and behavioral studies are examining the many factors that are believed to contribute to poor health in our communities. Understanding the cause of disparities in health is pivotal in determining and applying appropriate preventive, diagnostic, and treatment modalities.

Access to health care is a major health problem that potentially perpetuates health disparities. Those who have more resources are better positioned to benefit from costly new discoveries in science and medicine. An estimated 45 million Americans have no health insurance, most of them being racial and ethnic minority, rural, and low-income populations. A lack of access can delay timely medical care and increase the effects of disease without proper treatment. A study examining adherence to cervical cancer screening guidelines among publicly housed Hispanic and African-American women, found that only 62 percent of those sampled had received a screening for cervical cancer within the past year. 29 percent of the participants noted that no health care provider had ever notified them that they needed a screening test for cervical cancer. In this study, Hispanic and older women were far less likely to adhere to screening guidelines. The results prove the need for continued and increased efforts to ensure that medically underserved racial and ethnic minority women have access to cancer screening services. Understanding the complex nature of health disparities and the influence of socio-economic, biological, environmental, behavioral, and other factors, remains a research challenge that we must continue to examine through pioneering research.

TRAINING THE WORKFORCE: REMOVING THE BARRIERS

Access to health care is a multi-pronged problem that is complicated by the shortage of health professionals from underserved communities. Racial and ethnic minorities make up only 14 percent of the physicians in America. The NCMHD and its partners have been working to diversify and strengthen the science workforce through training. Two-year loan repayment awards have alleviated the financial burden of pursuing higher education for approximately 1,100 health professionals. These trainees with MD, PhD, DDS, and other doctorate level science degrees, engage in research, health promotion, and outreach activities in numerous disciplines to heighten awareness and deepen our understanding of specific diseases and conditions, and issues in health disparities.

Racial and ethnic minorities represent 64 percent of the current pool of NCMHD loan repayment awardees. An estimated two-thirds of the graduates have secured academic or research positions. The funding provided by loan repayments have helped to advance the careers of awardees and expose them to additional funding sources for their research activities. The program is slowly, but evidently achieving its mission to recruit and retain highly qualified health professionals in the workforce. In 2006, endowment funding supported the training of two Native American students completing the four-year Doctor of Pharmacy program at the University of Montana. This is a significant accomplishment because of the critical need to create permanent tenure track positions for Native Americans. At the University of Wisconsin at Madison, School of Public Health, the infrastructure established with NCMHD funding has helped to secure funds for a Health Disparities Research Scholars Training Program. This five-year training program will commence in Spring 2007 and it is anticipated that it will increase the number of researchers committed to health disparities. We will continue to enhance our focus on the recruitment and retention of individuals of health disparity populations to develop a culturally competent and well-trained workforce to address the burden of health disparities in our diverse communities.

CREATING THE COMPETITIVE-EDGE

The quality of health among health disparity populations, and the delivery of health care can be improved by training a diverse workforce that is representative of the community being served. However, in order to conduct innovative research, it is essential to have the right capacity such as the facility, faculty, students, and training programs. Notable progress has been made in developing research capacity at more than 40 academic institutions.

Having an endowed chair signals an institution's strength in a specific discipline. It is an incentive for a medical school to recruit and retain the most preeminent faculty in a given field, and adds credibility to its medical education program. En-

dowed chairs traditionally have been located at the most prestigious medical schools. NCMHD funding has established endowed chairs at three minority-serving institutions, Meharry Medical College, Morehouse School of Medicine, and the University of Hawaii. These endowed chairs are vital to building a critical mass of distinguished scientists in cancer, cardiovascular disease, diabetes, neuroscience, women's health, and Native Hawaiian health. This will place these institutions on the competitive edge to advance their study of minority health and health disparities in these fields. At Meharry, the endowed chair funds have helped to recruit a nationally renowned scientist to lead its Center for Excellence in Health Disparities Research in HIV/AIDS.

Research capacity in terms of physical infrastructure has increased considerably at several institutions after obtaining NCMHD funding. In some instances, facilities for health disparities research did not exist prior to NCMHD Centers of Excellence funding. Today, Charles R. Drew University has space totaling 8000 square feet, New York University 3,900 and Claflin University 3,403 square feet dedicated to conducting health disparities research. As a result, these institutions have been able to expand their research and training activities. The University of South Carolina-Claflin EXPORT Center recently erected a Molecular Virology Laboratory at Claflin University which houses state-of-the-art equipment for microscopic gene cell isolation and examination, where HIV viral load assays for example, can now be studied. The University of New Mexico houses the only School of Medicine in the state, and endowment funds have helped to establish the Institute of Public Health to address chronic health issues among low income and racial and ethnic minority populations.

VALUE OF PARTNERSHIPS

Our success in eliminating health disparities will ultimately depend on our ability to translate the lessons learned from our research endeavors, into usable tools and programs for the community. We have expanded our partnership base, and moved beyond the tradition of limiting partnerships to academic institutions, into domains where we can have the capacity to respond to health disparities in any form. We have continued collaborations NIH-wide, across the Department of Health and Human Services, and with other agencies such as the Department of Justice. Our efforts also have engendered unique partnerships between academia and the community; the community and local, state or federal agencies; research-intensive institutions and minority-serving institutions; and among NCMHD Centers of Excellence within a given state and state health agencies.

In partnership with the National Institute of Environmental Health Services, the private sector, universities and schools, molds and other allergens that may trigger asthma in children are being studied post-Katrina. In conjunction with the DHHS Office of Minority Health we mobilized our Centers of Excellence to respond to emergency health needs in the community and offer research opportunities at NIH for scientists after Hurricane Katrina. Today, the community is benefiting from electronic medical records, and telemedicine programs that are being incorporated into the health care infrastructure. In Oklahoma we have been able to reach more than 65,000 American Indians through a partnership of the Oklahoma Project EXPORT Center with nine tribes. The power and impact of our partnerships has touched the global community from state to state to places like Asia, Africa, Europe and the Caribbean where our students and faculty engage in research training.

IMAGINE THE FUTURE

We have begun to set the foundation through our research, training, capacity development, and outreach efforts to transform the health of this nation, but we have barely touched the surface. There is far more to be done. In three years, according to the Healthy People 2010 report, health disparities should be eliminated. However, the recent Midcourse Review of the report underscores the fact that not enough has been done overall to demonstrate any significant decline in health disparities.

Imagine a Nation where differences in health status and health outcomes no longer exist among populations. Imagine a nation where all Americans can lead a long and healthy life. Imagine a country where all Americans can access quality health care. Imagine physicians and health care professionals of all racial and ethnic backgrounds, in any specialty, practicing in every community across this country. Imagine cutting-edge biomedical research being led within our communities by members of the community. Imagine the discovery of solutions for critical diseases like diabetes, mental illness, cardiovascular disease, HIV/AIDS or obesity emerging from a community lab.

At the NCMHD we are cognizant that no single entity alone can solve the complex problem of health disparities. The sustainability and success of our health disparities efforts depends on strategic partnerships. We will continue to expand our network to address the diseases and issues that are already familiar to us, and examine new and emerging health disparities challenges in prisons, housing communities, or among our men. We must also be able to respond to health crises as they arise. Novel and multi-faceted strategies must be exercised and increased at the community, national and global level if we are to succeed in using the power of biomedical research to transform the health of racial and ethnic minority and medically underserved populations and eliminate the scourge of health disparities.

NCMHD PROGRAMS

Senator HARKIN. Thank you very much, Dr. Ruffin. I assume on this map you gave us, that CBPR, the green dot, is Community Based Participatory Research?

Dr. RUFFIN. That's correct, sir.

Senator HARKIN. We don't know how many are in each State. We just know there's something going on there, right?

Dr. RUFFIN. I think I can also tell you we've established 25 of those programs thus far. I think I have a map that I might be able to share with you that shows the distribution of those 25 programs.

Senator HARKIN. Tell me again what's that loan repayment program? How does that work?

Dr. RUFFIN. The loan repayment program is where we pay back the loans of individuals who go into health disparities research. These individuals get about $35,000 a year, principal and interest is paid as a repayment for those individuals to go into health disparities research. It is modeled a lot like the AIDS-Loan repayment program which many of you are familiar with, except in this case, our loans are given to not just MDs but to all health professionals.

Senator HARKIN. Would that be nurses too?

Dr. RUFFIN. Nurses, dentists, individuals in clinical psychology, sociology, all of the medical professions are eligible to apply for these loan repayment programs.

Senator HARKIN. Interesting. I have to find out more about that.

VACCINES

Dr. Fauci, I would like to talk a little bit about vaccines. As you know we have provided over $6 billion to HHS to prepare for a flu pandemic. A lot of that money is to develop both egg-based and cell-based vaccine capacity in this country. We've been through that many times.

But in the case of a pandemic even after spending this money, it will take us months to develop a vaccine that will be effective against the strain of flu that proves to be able to be transmitted from human to human. It will still take time.

UNIVERSAL VACCINE

Now, I've heard a lot about this idea of a universal vaccine. One that would be effective against all strains of flu, a vaccine that could be stockpiled now, made immediately available at the time of a pandemic or one that could be routinely administered to people giving them immunity in advance of a pandemic in certain areas.

I recently met with some people who were developing a DNA based vaccine that identifies proteins. It was very interesting to

me—that are common to all strains of flu. And I understand your Institute has supported some of this work. I just need to know more about this. Is there this possibility that we could get this universal vaccine that—since we identify proteins that are the same in all the different flus? Is this possible?

Dr. FAUCI. It is conceptually possible. I think over time it will be likely.

When you look at a flu virus the major components that we traditionally over the years have made vaccines against, have been the H and the N proteins that are on the surface. They stand for hemagluttinin and neuraminidase. That's the reason when you hear about flu—you name flus by the differences, H5N1, H3N2.

Now the good news is that the body makes a really good immune response against the H and the N. The bad news is that the H and the N change from influenza to influenza. Which is the reason why each season, to get a perfect match, most of the time you have to fine tune and tweak the vaccine a bit so that it's a little bit different than the one you did the year before to get optimum and maximum protection.

The concept that you're referring to, Mr. Chairman, is the idea of getting the components of the virus that don't change from strain to strain and season to season. Two of those proteins are the M2 or the matrix protein, and the NP or the nuclear protein. They don't seem to change from strain to strain. So then you—you ask the obvious question. If I was infected with seasonal flu 3 years ago, why am I not protected against the seasonal flu the next year or the year after?

The reason is the body does not make a very robust immune response against the M protein and the NP. So the strategy that we're working on with the people that you mentioned is to get those proteins and put them in a very immunogenic form. So that the body makes a very robust immune response that would cross over and help protect not only against this season's flu, but next season's flu and the year after.

Also, theoretically if you do it right, you could get a universal vaccine that would even be protective against a wide variation. The way we're seeing with the H5N1. Because the H5N1 that's circulating in birds in south east Asia right now, is very much different from the H3N2 that we all get exposed to every season. So that's the concept and the strategy of a universal vaccine.

The results that we're getting, preliminarily, in animal studies are really rather encouraging. Now you know in vaccine work it takes years to go from the concept to something that's in a bottle for people to use. But, I, myself am quite encouraged about that possibility.

Senator HARKIN. So you're funding research on this?

Dr. FAUCI. Oh, absolutely. We're funding research by our extramural grantees and contractors. We're collaborating with some of the pharmaceutical companies. For example Merck itself is working on a M2 vaccine. We're doing intramural research.

You mentioned the DNA approach. Where you can take the gene of any particular protein and code it for the protein that you want and essentially say I'm going to inject somebody with the DNA. That DNA will then cause the body to express the protein on a cell

that makes a good immune response. At the Vaccine Research Center under Dr. Gary Nabel, at the NIH, that's what we're doing with HIV. It's easily done also in influenza.

FUNDING INFLUENZA VACCINE RESEARCH

Senator HARKIN. Do you think we're putting enough resources into that on the balance of things? This is very promising.

Dr. FAUCI. It is very promising. It's very promising.

Senator HARKIN. It would be a big deal.

Dr. FAUCI. It would. It would. As you know I've always told you over the years you never ask a scientist if you put enough in. Enough is when you get the answer. We are putting a substantial amount. We are concerned as we all are with—when we have a flat budget will we be able to take advantage of some of the opportunities that would arise. So we have to be very careful in our prioritization. But we're putting substantial resources into it.

VACCINES AND AUTOIMMUNE DISEASE

Senator HARKIN. Two other things. I just want to ask one about vaccines and I want to ask about allergies.

Children get a lot of vaccines by the time they're three years old. I've heard estimates ranging from 18 to almost 30. Having a new grandchild myself last year, their parents are looking at all the shots that this kid is supposed to get by the time they're, well, 1 and then by 2. It was pretty darn close to 30.

I've heard a lot of concerns. That, you know—while each of these vaccines are very good in terms of saving lives, building immunity that maybe collectively, putting them all together could lead to autoimmune diseases later in life. I've heard a lot of this, read about it. So, again, I want to know, what kind of research is being—done on that aspect of all of these together effecting autoimmune diseases later in life?

Dr. FAUCI. It's obviously a good question because it is a matter of concern to some people. There have been studies done looking at retrospective data of children who get vaccinated as to whether or not there's this propensity to autoimmunity.

The basis of that concern, I think is the basis of why you really do want to vaccinate people because in people who have a genetic predisposition to autoimmunity, it is often triggered by an infection. We know that, for example with certain of the autoimmune diseases like lupus and rheumatoid arthritis and things like that.

So the question is mimicking the infection by a vaccine going to induce autoimmunity. The answer is in studies that have been pretty carefully done, no. But, importantly, the infection itself is a much more potent potential inducer of autoimmunity than is the vaccine that you give to somebody to prevent the infection.

So if we didn't vaccinate people and they actually got these infections that would be an even worse scenario. So if you're asking me, I can give the example: I have three children and they've gotten all the vaccinations. I feel very, very comfortable with having my children vaccinated with the menu of vaccines that are all recommended.

So, the concern is understandable. The research in the studies that have been done to see if there is a connection have all indicated that there is not.

FOOD ALLERGIES

Senator HARKIN. One last thing, allergies. A friend of mine in Iowa—we're just talking about kids and our kids, grandkids. It turned out that their little boy had developed severe food allergies.

You and I have talked about this before in previous hearings. Three hundred percent increase in the number of pediatric food allergy cases over the past 10 years. That's alarming.

Dr. FAUCI. Yes.

Senator HARKIN. What's going on? You know, what is happening out there?

Dr. FAUCI. To be honest with you, we don't know. There are some theories about that, but food allergy is something that we have now, we have had for some time. But even most recently based on the data you're talking about, are taking it very, very seriously.

Not only is food allergies—and certainly the recognition of and probably the reality of, more than just the recognition of are increasing. Not quite sure why that has occurred. I'm certain that there are factors that are not fully appreciated by us right now. But the thing that worries us is that some of these food allergies are more than just trivial. You can actually get anaphylaxis. One of the important ones, for example, is—is peanut allergies is really, really tough.

PEANUT ALLERGIES IN CHINA

Senator HARKIN. I've heard. Now tell me if I'm wrong on this. Have you ever heard this about kids in China eating a lot of peanuts there. But they don't get peanut allergies. But we get peanut allergies here. Have you ever heard such a thing?

You haven't heard that one?

Dr. FAUCI. I haven't heard that but I thought you were going to say that the Chinese were putting something in it that is toxic.

Senator HARKIN. No, it's just that China grows a lot of peanuts, like ours. The kids eat a lot of peanuts. But they have nowhere near the peanut allergies we have in this country. I was operating under the assumption that was factual data. I don't know.

Dr. FAUCI. I've not heard this.

Senator HARKIN. Look into that.

Dr. FAUCI. I certainly will. I certainly will.

RESOURCES FOR FOOD ALLERGIES

Senator HARKIN. But—again, with the 300 percent increase do we have enough resources going into that? It's our resources again.

Dr. FAUCI. It's the same answer to the question. We are doing a substantial amount. We could do more. Definitely.

Senator HARKIN. I'm told that NIH hosted an expert panel on food allergies in the spring of 2006. Last year. The participants developed a proposed road map to guide future research. But it has been a year now and I understand the road map still hasn't been approved. Give me an update on that, would you?

Dr. FAUCI. We met with that group in my conference room about 3 months ago. We walked away from that with them. They are quite satisfied with the portfolio that we've put together. With regard to a strategic plan that's almost a logistic thing, about getting a plan and a plan approved through the Department and what have you.

But the research that we're doing right now on food allergy, we've developed a very good relationship with the constituency groups on that. I have a lot of responses to that meeting that were very favorable.

Senator HARKIN. Well, alright. I just wondered what was happening there. I just—you can jump in anytime, just jump in if you have some things you want to cover. Go ahead.

COORDINATION WITH DEPARTMENT OF DEFENSE

Senator STEVENS. Tony, what about coordinating what you're doing with the other agencies? We're putting a lot of money in defense for investigation dealing with substances that might be used by terrorists for instance. Are you working with them too?

Dr. FAUCI. Yeah. There is a rather excellent coordination, Senator Stevens, between ourselves, the Department of Homeland Security and the Department of Defense. In fact, we feel very good about that. We were doing that—we've developed a good relationship with them.

Even antedating bio-defense because a lot of the things that they have done for force protection, malaria, and things like that, we have worked very closely with them. When the bio-defense issue arose following 9/11, we, in fact, strengthened our interaction with them. With the new Department of Homeland Security, we're even coordinating very nicely with them.

BIOLOGICAL, RADIOLOGICAL, OR CHEMICAL ATTACK

Senator STEVENS. That was going to be my next question because it just seems with the world wide impact of the terrorist movements that they're going to turn to substances one of these days. Are we prepared for that?

Dr. FAUCI. We are not totally prepared. I would be misleading you if I told you we're totally prepared for any biological, radiological, or chemical attack that we have. But since 2002, we have built up a rather robust research and development portfolio and have made some significant advances.

Obviously, you never know where, when or if a terrorist is going to strike in a biological, radiological, chemical way. But we have countermeasures now that we didn't have before. We were completely vulnerable to a smallpox attack. We had 18 million doses of smallpox vaccine in our reserve. Right now we have over 400 million. That's happened just over the past couple of years.

Senator STEVENS. That was my next follow up because it seems to me that we're doing a lot of research and prevention, but what about reaction to such events when they take place. That seems to be the area that we could be most effective.

Dr. FAUCI. Right.

Senator STEVENS. We can't immunize everybody against anything.

Dr. FAUCI. Sure.

Senator STEVENS. But we can get prepared for specific problems that might arise. Are we doing that?

Dr. FAUCI. We are. We are, Senator. I'll give you two examples that are actually very important examples.

You talk about treatment. We've never had any treatment for smallpox or pox viruses. There is a drug that we've helped develop with a pharmaceutical company called ST–246 which is very effective in an animal model against smallpox. You may have read in the newspaper about a military person who was getting vaccinated for smallpox with vacinea didn't fully realize that his child had eczema. When you expose the wound of a smallpox inoculation to a child with eczema, they can get an eczema vaccinatum which is a very terrible disease.

The child did get it accidentally, and doctors tried everything with the child and we brought this drug in. They treated the patient with the drug and the child has made a very remarkable recovery. So that's a—N equals one in medicine that doesn't mean anything, but this, I think, is an important indication that we now have an important drug.

We also have some antitoxins that we didn't have, for example against anthrax. We've developed the first Ebola vaccine that, I think is a very important advance.

Senator STEVENS. What about post exposure to nuclear. I heard the other day about something that would reduce the after effects of nuclear exposure.

Dr. FAUCI. Right.

Senator STEVENS. Is that really an accomplished fact.

Dr. FAUCI. What we are doing and we've had to partner with our colleagues from the cancer community, with the National Cancer Institute is to develop better versions of the drugs that are used on patients following a radiation to rescue bone marrow. For example, to allow the bone marrow to regenerate in a much more rapid and efficient way than it would to wait for it to normally respond. That's the main nuke-rad counter measure that we have.

Senator STEVENS. Are we stockpiling that?

Dr. FAUCI. Yes, we are. We have that in the National Strategic Stockpile.

NCI FUNDING

Senator STEVENS. Dr. Niederhuber, if I may? I was really—you know we doubled the research money for you in one period that Connie Mack and bipartisan effort. We did that over one period. I think it was a little less than 10 years. Are we going to look at a necessity to double it again in the next decade?

Dr. NIEDERHUBER. Well, living as we have for the past 3–4 years with a less than inflation budget has certainly taken its toll on the programs. If you calculate that up it's about a 12 percent decrease from where we might want to be at this point.

Senator STEVENS. Well, since you had 125 percent increase in the past years before that. Where do you think you'd stand if we hadn't done it?

Dr. NIEDERHUBER. Oh, I think we would be much worse off in the country as a whole. I think the increase that Congress, in its

wisdom, legislated and appropriated did a great job in this country in building up research infrastructure that was lagging. We built about $16 billion worth of new research space at our Research Universities across the country. I think that was badly needed.

Having come recently from the academic community we had some real pent up needs in the academic community. We were able to increase our faculties where we needed to in the biomedical research arena. So I think this was all, Senator Stevens, very needed.

The issue I think for us, as a country, has been that when you build up you need to keep moving with inflation in order to maintain what you've built. I think that's the issue that we are facing.

GENERATIONAL CANCER

Senator STEVENS. That's reasonable, I think.

Let me ask you a personal question. I had three generations of pancreas—pancreatic cancer ahead of me and I got prostate cancer. Now someone told me the other day that in all likelihood I had the same cancer. Is that possible that it migrated to my predecessors but didn't migrate for me?

Dr. NIEDERHUBER. Well, I don't think I would look at it quite that way, having been involved with managing and operating on patients with pancreatic cancer for most of my career, I think these are two separate diseases. They each have specific risk factors. I could share that with you.

Senator STEVENS. I just want to know what to tell my sons.

Dr. NIEDERHUBER. Well, I think the thing to tell your sons is that we're working hard to better understand the risk. What I was going to say that actually in July of this year our Center of Excellence in the National Cancer Institute focused on trying to understand risk in populations and risk for developing different cancers. We've just finished a whole genome scanning project in prostate and in breast and this July we'll launch one specifically in pancreatic cancer. So it's relevant to your question, Senator.

Senator STEVENS. Well, let me know will you?

Dr. NIEDERHUBER. I certainly will.

Senator STEVENS. What do I tell them—follow their grandfather, their great grandfather?

Dr. NIEDERHUBER. Live healthy, exercise, eat well.

ATTRACTING STUDENTS TO SCIENCE AND TECHNOLOGY CAREERS

Senator STEVENS. Which one should they be careful of? Anyway, let me ask you, Ms. Alving.

Are you familiar with Norm Augustine's report titled: "Rising Above the Gathering Storm", which discuses the problem of having enough students turning to the study of science and technology?

Dr. ALVING. Yes, Senator. We're very aware of this at NIH.

Senator STEVENS. But what are all of you doing about that? All of you have basic money, research money. I understand what you're doing Dr. Ruffin. That's very good.

We do the same thing by the way. We pay some of our staff who have high loans, before they migrate out to where they get paid more. So we have a little bit of a fund here. We can sort of entice them to stay a year or two longer. But are you doing anything about the concepts of trying to attract students into the areas so

that you're not the last of the breed in terms of scientists who are studying these things for us?

Dr. ALVING. Yes we are, Senator. I would say that NCRR is working very diligently on this. The other Institutes and Centers are working on this, as well, because across NIH we recognize this as a very large challenge. We also recognize——

Senator STEVENS. Let me interrupt you. Do you have internships for people in college to attract them so they'd be interested to go to graduate school? Do you reach out to people?

Dr. ALVING. Absolutely. For example, let's look at the IDeA program that I mentioned earlier. I personally visited Montana this last year and I saw how the investigators at the more research intensive universities are reaching out to the tribal colleges. So there are now research projects underway at the tribal colleges. The tribal students can go to the University of Montana and really envision research careers.

I remember one young man told his father he was going into biomedical research. He was Native American. His father said well, that's not what we do. But he said yes, this is what I do want to do.

So we are reaching out to students, I would say, of all ages, because to really attract students into research and into biomedical careers, you really have to get them at a very young age. In one of our SEPA programs, our Science Education Partnership Awards, one of our very fine investigators has developed a bus in Boston that actually is well equipped as a laboratory. It's even visited the NIH campus.

The bus goes throughout Boston. So it goes into the underserved areas. Students can get onto this bus, which is a traveling mobile lab, and learn about DNA and learn some of the simple experiments. In fact, I think this has been really replicated throughout many of the States.

So we're really attacking this, I think, at multiple levels. We're reaching out to the Hispanic community as well. And many of our very well funded researchers have very active programs where they serve as mentors and bring high school students into their labs. It's probably still not enough, but we're all very aware.

Senator STEVENS. If this Nation has a problem—the problem is the downward trend of our students who seek graduate education in science, technology, and engineering, which are very difficult areas of study. We've got to find some way to move out and give them incentives to continue.

CONGENITAL DEFECTS

I know I'm using my time. Dr. Grady, I just recently came about in connection with a relative. The problem of a defective heart valve which came from, they tell me, from what you mentioned, a problem at birth. Now what my question to you is have we any way to check this as people grow older? Whether they do have those defects that develop because of improper handling at birth?

Dr. GRADY. There are a number of tests that are now available where we can through imaging and other diagnostic tests tell very early on in children if there is a developmental defect.

Senator STEVENS. I'm talking about this person's almost 60. He was just determined—to have blood clots going to the brain. Suddenly they find out that was—escaped through some valves that have been defective since child—since birth. Now I—and he's had exams. He's been in the service. Why doesn't—why won't that show up on exams?

Dr. GRADY. Well, it turns out that many of us have problems, birth defects, congenital defects that we are really unaware of. Sometimes we die without being aware of them. But now that the life expectancy of the average American is longer, many of these things which would not have surfaced before are now surfacing.

Senator STEVENS. But how can we—can we discover them?

Dr. GRADY. Up until recently the imaging technology and the other technologies that we had were not able to. But we now have imaging technologies which have a very high resolution. You can tell things are happening in tissue that are structural and even metabolic disorders much earlier in life.

Senator STEVENS. Those valves could be discovered with the proper test?

Dr. GRADY. Yes. Very likely they could have been.

Senator STEVENS. Are we developing any indications that would lead people to take those tests?

Dr. GRADY. Actually there is a move on for people to do screening, whole body scans, et cetera and much higher technological screening early on in life. Some of these things, as we're all aware of, are not covered by insurance so people opt not to do them. But I think the technology is now becoming available and people's awareness that they should screen for things and that they should have check ups early is much higher. So hopefully, we'll be catching these earlier.

Senator STEVENS. We saw something that both the government and the insurers are not going to pay the cost of scans, particularly full body scans.

Dr. GRADY. That is currently the situation. There is a great deal of discussion, whether or not they should be available and for what particular conditions they would be most helpful.

MEDICAL SCREENING

Senator STEVENS. This is very disturbing. This person is now blind, partially. He's got tunnel vision because of those clots and had no idea that that existed. I was told it could have been diagnosed at any time prior to that if he had had the proper exposure to the scans. But I don't know how.

We've got all these systems. I don't know how we can get so that subjective to the people who need help, know that need help. Is that part of any of the studies we're making? How do we find out who needs this help?

Dr. GRADY. It is a problem in that we are trying to inform people. But we also have difficulty getting people to come in for screening exams which we know are helpful: mammography, breast cancer screening, and there are a number of other screenings that people do not necessarily take advantage of.

We are studying—we're funding a number of studies however, that look at what it takes to get people incentivized to come in for

screening. We have some very interesting information related to, you mentioned relatives, related to mothers and daughters. Daughters being more tuned into health prevention, getting mothers to come in, senior citizens and younger people, et cetera. So we're working on a number of techniques to incentivize people to come in for screening.

Senator STEVENS. I was told last week that there is now a system where you can go and have your—what your gene chain set out. They can compare that to the types of illnesses that come from these genes that you are determined to have and they can then give you a prediction on what you're going to suffer. I said why don't we all get that? They said, well, it's cost. That it's not available to the average income person today. Are we going to get to where we can get that for the average person?

Dr. GRADY. Well, it is true that it is not covered by insurance but also—we're not quite there yet where these tests are 100 percent accurate.

For some things such as stroke, we have developed and identified risk factors. We can weigh each one and there's a whole scale where you plug in your blood pressure, your age, et cetera. Then you can alter—what if your blood pressure came down a certain amount and you get a score which you can then program. If I alter my diet, if I lower my blood pressure, if I exercise more, that will reduce my chance of getting a stroke by *x* percent or so many points. So I think we are moving in that direction in some areas, but we're really not there yet.

Senator STEVENS. Maybe some of us don't want to know that's the problem.

Senator HARKIN. Do you have thoughts on what Senator Stevens just asked?

Dr. NIEDERHUBER. I was just going to comment that we—all of the Institute Directors were at a conference all day on Friday at the NIH and during that day we were talking about some of the latest technology coming online to do rapid sequencing. I believe, you can correct me, colleagues, if I'm wrong, but I believe the quote was that, "with this new technology today we can sequence half of our genome in 3 days at about $3,000."

So you can see how quickly within the next few years we will be approaching our goal of being able to sequence the entire genome of you as a patient within 3 or 4 hours for $1,000.

Senator STEVENS. Would it be cost effective for us to do that publicly?

Dr. NIEDERHUBER. Well, that's a very good question, Senator. I think that we all recognize in the science community that this information, this alphabet if you will, is the base of the information. We know that we have a lot more work to do in taking that code, if you will and understanding what that code means in terms of the proteins that our cells produce.

The changes in those proteins as they're produced and how they relate to what makes you function and you as an individual and your diseases and me, as an individual and my diseases. So we have a lot to build on. But that is like the periodic table of chemistry, if you will. It is the information based upon which we will

gain this kind of knowledge and this kind of understanding of the disease. It's a step, but a very important step.

GENOMICS

Dr. FAUCI. Can I add we should be careful though not to think that if you—if we, even if we get it inexpensively that if you get your genome and you look at your sequence, you're going to know exactly what's going to happen to you. That's—most diseases are multigenic. They rely a lot on interaction between the genetic factors and the environment.

So although you could get some probabilities there's still going to be the need for the broad, healthy things you need to do no matter what your genome is. So we spoke about that also.

Senator STEVENS. I said it was the last question. But I forgot this one.

END OF LIFE

Dr. Grady, you gave us this chart, tracking patient disability in the last year of life identifies opportunities to tailor interventions. We were told last year that in the last 2 years of the person's life they would probably spend as much money for health care as they've spent in all previous years. Are you suggesting here that there's some way to alter that?

Dr. GRADY. Your statement is true. What we are suggesting is that these are trends. So it's a very large population study but it gives parameters within which you can better be able to predict what a course of illness may be like. That doesn't mean it will necessarily be that way for each individual person, but it gives you parameters.

So it gives you a sense of what one could expect and hopefully to be able to better plan. It's an imperfect system when translated to single individuals but it does give the patient, the family, and the health care team some idea.

Senator STEVENS. Are you suggesting you think science can tell us when a disease is really terminal no matter what happens?

Dr. GRADY. We're still not there yet. It's very difficult. You can, as we all know, predict within some time frames. But still individuals are very different from person to person. So you have guidelines, but I would not be offering a finite timeline.

Senator HARKIN. Well, I want to pick up a little bit of what Senator Stevens just said this end of life care. I just wrote it down here. It's got to be more rational, caring and cost effective.

A lot of it is just irrational. The way it's administered. I don't know if it's more caring for a person to—to do expensive operations or anything like that knowing full well that the end of life is coming anyway than it is to just give him palliative care. Address yourself to that too.

Most—our health care system is not very good when it comes to palliative care—and then so a lot of people stay in acute care until they die. It just costs a fortune.

Dr. GRADY. It's very complicated, Senator, both Senators. What we found out so far—we've just scratched the surface.

What we've found out so far however that is disturbing is that some of the things that we could do we are not doing consistently.

For example, pain management. We know a great deal about pain management and our ability to handle pain in these stages of life. Yet, we find great disagreement between what the health team advises, what the patient says they want and what the family says that they think the patient wants.

So whether it's an intensive care unit setting or a hospice setting or chronic care setting, we find great disagreement. This is all within the therapeutic window of pain medication that could be administered that would be safe to administer. So that's one thing we know.

The other thing we have found is that—that many patients do not have advanced directives. They haven't really thought ahead. They haven't talked with their family, but even if they have many of the systems that we have are required. They basically are not allowed to withhold treatment, even if that is the patient's request.

So if in an emergency the ambulances are called or anything, it doesn't usually matter in practice if the person says no advanced measures.

Senator HARKIN. What would you think about that? I've never talked to Senator Stevens about this but this idea of having advance directives? People don't. They just don't think about it. Maybe when people get on Medicare that ought to be a part of when you qualify for Medicare that you ought to have a requirement that you have some kind of advance directive.

Dr. GRADY. Well if the person would have an opportunity to do that it would at least allow them to think about it. It would give the family some sense of where they should go and some guidance. It turns out the other studies we've done that look at the caregivers of terminal patients that the largest stress for them is reported to be that they didn't know what their family member wanted. They had to make a decision really acting in the dark by their report. That they felt was, by their report, almost as stressful as seeing the disability.

Senator STEVENS. But is that partly related to the liability factor of the caregiver in case another person—family member says you could have saved them and you didn't.

Dr. GRADY. There seems to be a great deal of anxiety about that.

Senator STEVENS. Well, I think, Senator Harkin is right. I think we ought to try to do something. I witnessed my first father-in-law after he had brought back to life. He was a minister and a grand man. He was in his mid 90s. I never heard him swear in his life, but he swore at the doctor that brought him back to life. He died about 2 months later and I think that is a very unfortunate thing. He did not have a directive. But there ought to be something to deal. Maybe we could tie to Medicare.

Senator HARKIN. I've thought about that. I hear this all the time. There is a liability problem there. People don't think about it. Families don't know what to do.

Senator STEVENS. I see my friend is here. I'm late for another appointment. So thank you very much, Senator.

Senator HARKIN. Thank you, Senator Stevens.

I want to follow up on one thing and that's on the nursing shortage.

Dr. GRADY. Yes.

NURSING SHORTAGE

Senator HARKIN. We had a hearing on global health a few weeks ago. We talked about the brain drain and other countries.

What's happening in other countries is a lot of their nurses especially in health care professionals are getting their degrees and that kind of thing. Then they come here, better paying jobs. We have a shortage of nurses here now so we started looking into this.

Well then, what did we find out? There's a shortage of nurses in this country. There's a demand for nurses. American Schools of Nursing last year turned away 42,866 qualified applications for baccalaureate and graduate programs due to a shortage of nurse faculty.

Dr. GRADY. That is correct.

Senator HARKIN. Now, we're in a real problem here.

Dr. GRADY. We are.

TRAINING NURSE FACULTY

Senator HARKIN. We need more nurse faculty. But if we don't have the slots for them, it seems to me pretty soon, they're going to start retiring and we're going to have fewer and fewer. I don't know.

Your Institute supports a lot of nurse faculty through research grants. So what role does your Institute play in increasing the number of nurses trained here in America, especially teaching nurses, faculty—teaching nurses? I don't mean just nurses that are out in the community, but I mean teaching.

Dr. GRADY. Senator Harkin, those are the nurses that we support in our training line. We have 7 percent of our budget devoted to training.

Senator HARKIN. 7?

Dr. GRADY. Yes, 7 percent, which is twice the NIH average. So we're dedicating a reasonable chunk of our budget to training. The people that we train are those individuals who become the teaching faculty. We train them to do research, but that's what faculty do on campuses of Schools of Nursing across our country.

So we have designed a number of programs to try to get these students in early. We work with the K through 12 programs. We work with the other graduates to encourage them to get doctorates. We also have what we call fast track programs so that they come into the baccalaureate program, come out with their Ph.D. without stopping.

Senator HARKIN. Thank you. What if you were advising us? If you could say here's what we're going to do. What would we do say; give us 3, 5 years. What would a 5-year plan look like to get more teaching faculty in this country?

Dr. GRADY. I think the 5-year plan would have some loan repayment, but I think that looking at loan repayment or service repayment. For example and this dates back to the older days, but we used to, if people had supported education that they would not have to pay back the loans, but they would pay back in service, teaching at schools as faculty, et cetera. I think maybe something of that sort.

Incentives to get people into the field earlier, I think there is a real sense and this is partly what we're working on internally is people are expected to get their advanced education but they're expected to work along the way because it is clinical profession. So we are trying to help design programs so that that is not necessary.

Believe it or not, many States require, in order to teach in a School of Nursing, that you have to have a Masters in Nursing and not just get your Bachelor's and then go on to a Ph.D. So there are a number of issues that we're working on. But it is safe to say that that the demand over the next 10 years is going up in excess of 20 percent. We're only supplying another 6 percent.

So we need programs that are attractive. We need programs to help retention. We have programs to help get people in but we need to figure out how to retain them. I think we need also to work on the quality of life issues such as loan repayment.

Senator HARKIN. Well, we need some advice. I mean if you turn away 42,000 last year. I assume the same will happen this year, maybe more.

Dr. GRADY. Yes. We are, as you had identified very astutely, expecting an increased retirement. It turns out that faculty in Schools of Nursing tend to retire earlier than later, 62 versus 65 or so on. So we really are getting a crunch from several directions. So we're hard pressed to try to design as many programs as possible to get people in and to make the field as attractive so that they will stay in.

NURSING RE-ENTRY

Senator HARKIN. Let me ask you this. I was amazed to discover in my State of Iowa a few years ago that there are a lot of nurses in my State, and I'm sure it must be true in other States. They went to nursing school. They became an RN. They were an RN for a while. They got married, started having families. They got out of nursing, raised their families. Kids are grown. They may not have been in nursing for 15, 18, 20 years. I was amazed to find out how many there were in my State.

So I began asking a few of them once I found out. In meeting people you never knew they were nurses. You meet them in other walks of life and find out they were a nurse. Would they ever think about going back into it. And they said, Oh, yes. But you know I don't, you know, have the wherewithal. It costs money to get retrained, go back to school. You know we're now in our late 30s, 40s. You know, yeah, if I had the ability or had the financial resources and stuff.

I just wonder if there's an untapped pool out there of nurses who may be in their late 30s, early 40s that would get back in if they had the wherewithal to do so.

Dr. GRADY. I believe there is, Senator. We've been talking with some of the schools about a re-entry program and with the AACN about re-entry programs. That is precisely what you're describing. To get people to come back in, if they have incentives.

You know it probably would not take a great deal of incentive. But to get people to think about it and to try to figure out some creative ways to get people back into the field. It is a wasted re-

source. Basically if people would like to come back to work, they have the background. I think it's an untapped resource.

Senator HARKIN. We ought to look—we ought to just see if there's some suggestions out there.

Dr. GRADY. I'd love to—we'd love to work on this, with you.

SUPPORT FOR WOMEN PURSUING PROFESSIONAL CAREERS

Dr. ALVING. The reason I'm nodding my head is that if you look at medical schools now, about 50 percent of the students in medical schools are women. We have a very big problem in this country in that there's very little support, child care support for example, for women who are trying to pursue professional careers. So this pertains to veterinarians, of whom 80 percent of the students are women, nurses and now physicians.

So I think we're going to have to think about some sort of ability to provide resources, child care, for those professional women. These nurses might not even drop out. They might stay in if they felt that their families and their children could have the appropriate type of child care.

Other countries have organized centers where they can, you know, provide day care. So that's another component of it. But I do support re-entry. I would also support it if they could only drop back to half time and not drop out, because once you drop out it's harder to re-enter. You lose confidence and that's a little bit more difficult.

Senator HARKIN. Interesting concept. I'm justified that the programs—programs for specified for certain groups like nurses. That's interesting.

Dr. RUFFIN. Senator Harkin, I think one of the areas too where we need to pay more attention is to our 2 year institutions around the country. This is an untapped resource to a great extent. I think that the attitude as it relates to 2 year colleges around the country has changed.

It used to be that the thinking was that individuals would go to the 2 year institutions to sort of bone up for the 4 year experience. That attitude is totally gone. We have great instructors now at these 2 year schools and good students at these 2 year institutions.

The problem is we're not bridging them. They're not transitioning to the 4 year institutions. We need more bridging programs that we can tap that vast resource of individuals who are at these 2 year institutions and begin to bridge them into our 4 year institutions in those challenging programs like nursing.

That's one of the areas that I think we need to concentrate on. It is a place where we need to visit that we haven't put much attention on.

Senator HARKIN. Very good. Dr. Niederhuber, let me ask you before I just turn to Senator Cochran.

I just wanted to ask you about clinical trials. Flat budgets for NCI over the past few years have taken a toll on clinical trials. When we finalized the fiscal year 2007 budget earlier this year, NCI was asking the cooperative groups that run cancer trials to trim their cost by 10 percent and reduce the number of open slots for patients by 3,000. Are those figures still accurate? I mean we did put some more money, as you know, in.

Dr. NIEDERHUBER. When we were trying to guess what that 2007 appropriation might be we were forced to ask everyone to do a worst case scenario. So they did work on a 10 percent cut. We actually, just the past few days, have been meeting together at NCI to put in place our funding program for the cooperative groups that are the bulk of the grants that support clinical trials research across the country, as you know.

It looks like it's going to be closer to a 5 percent decrease from last year. But that still translates into a decreased number of trials that will be open and a decreased number of patients that will go on trials as you understand.

One of the difficulties with this uncertainty in the budget for the clinical trials aspect of research, it's complicated to explain, but part of the support goes for infrastructure, bio-statistics and just the infrastructure people that have to be there. Another part of the budget is a bit of a guess in that we set aside resources that pay on a per patient basis. So as a patient goes on trial, that capitation gets allocated to cover part of those costs. It doesn't in any way cover the cost of a patient going on clinical trial. We're lucky in most trials if we come even close to 50 percent of the cost.

So, the problem the community at large is facing across the academic universities is not knowing exactly how that budget is going to grow or stay flat over the next few years. They have to be very careful on deciding to start a trial, get it up, and get it in place. That takes time and commitment. Not knowing for sure if the dollars are going to be there to support that trial in the second, third, and fourth years.

One of the things we do not want to do is to have to stop a trial in the middle. That would be a disaster. We just wouldn't want to do that. So I think that what I am seeing is that my community is being a little cautious in the number of trials they're willing to open up and willing to start because they can't predict down the road 2008, 2009, and 2010, what the resource flow is going to be.

Do you follow that? It's a complex issue. It's hard to explain a little bit until you get your hands into it.

Senator HARKIN. But you can assure that this 10 percent cut is no longer valid because of the——

Dr. NIEDERHUBER. It's not going to be that much in 2007. It's going to be closer to 5 percent.

Senator HARKIN. We need some kind of—I'll have to think about that a second. I have a question about pancreatic cancer, but I wanted to turn first to Senator Cochran.

Senator COCHRAN. Mr. Chairman, thank you very much for convening this hearing.

It is good to meet with the heads of the different Departments at NIH where you're undertaking very important research. We appreciate the hard work that all of you are doing.

We want to be sure that the budget request is as generous as it can be as well as the appropriations that follow. That when we approve a budget for this next fiscal year it reflects our genuine concern about doing the best we can do in developing research programs that will give us answers to problems relating to health and disease, infectious diseases, all the gamut of subjects that the Institute is working to help us understand.

PANDEMIC FLU AND OTHER INFECTIOUS DISEASES

I noticed that in Dr. Fauci's National Institute of Allergy and Infectious Diseases, you're doing a good bit of work in Avian flu and some other areas of that kind. I wonder what progress, if you can tell us is being made in coming up with new ways of dealing with some of those challenges of infectious diseases.

Dr. FAUCI. Well we have a very extensive portfolio in emerging and re-emerging infectious diseases, as you know. That is a major component of what we do. You mentioned pandemic flu and the concern that we have now because of the activity that is going on with bird flu particularly in south east Asia.

What's happened over the last year since I testified before the committee is some significant advances in that regard. We tend to link, Senator Cochran, our preparedness for seasonal influenza with that of pandemic. We feel as a group that we don't prepare well enough for seasonal flu. We have not advanced the vaccine technology for seasonal flu. The shots that you and I get every year that everyone else gets every year or should get every year, we haven't advanced that technology to the 21st century. We really need and we are not only re-looking at it but really transforming it.

For example, we make influenza vaccines now by growing them in eggs and then harvesting the virus in a very antiquated process which has great restrictions on scalability and the amount you can make. We've invested a lot of money to get the more up to date, 21st century methodologies for vaccine, either growing it in cells or doing recombinant DNA technology. We've made some significant advances in that regard.

I mentioned before you came in that the pre-pandemic influenza vaccine for H5N1 that we tested over the past couple of years has now been approved by the FDA as a licensed vaccine. What we need to do and are doing rather successfully is applying, for example, the technology of adjuvants, which is a substance which enhances the body's response to a vaccine so you can get away with a much lower dose and can scale up rapidly.

So I would report to you today that the work on emerging infections in general but in particular with regard to your question about pandemic flu is coming along very well.

HEALTH DISPARITIES

Senator COCHRAN. That's very encouraging. We appreciate the good work that you're doing. I noticed in one of my staff memos here that a recent report indicated that one of our counties in Mississippi has the highest mortality rate from breast cancer in the Nation. That stopped me. It's twice the national average in Madison County, Mississippi.

I wonder, we've talked about disparities. I think this might be something that the Research Centers in Minority Institutions program may be involved in. Dr. Alving, I think you'd know about that and can contribute something to our knowledge about what progress we're making at the National Center on Minority Health and Health Disparities.

Dr. ALVING. At the National Center for Research Resources we fund the RCMIs, or the Research Centers in Minority Institutions. We also work with Dr. Ruffin of the National Center on Minority Health and Health Disparities. I think also at the NCI there is a very big program in minority centers in cancer outreach.

I would wonder if there isn't a multi-factorial reason for this high mortality. The first question would be is it due to lack of screening. Second we would want to know that if there are women who have increased breast density which can also affect the screening results or the mammography. But I would really wonder about access to care and preventive measures.

As you know, the NHLBI funds the Jackson Heart Study in Mississippi, which is not only an observational study, but is dealing with ways of getting the participants used to the idea of preventive care and screening. We and the Research Centers in Minority Institutions are setting up a translational research network, with Jackson State as the data coordinating center, where we can do improved outreach and clinical trials in minority populations and also work collaboratively with my colleagues here at the table.

Senator COCHRAN. Let me ask Dr. Ruffin to comment on that too.

Dr. RUFFIN. Senator Cochran, I think that first of all what I would like to do is really congratulate the people in the State of Mississippi, if you're looking for an example of partnerships.

I just believe that whatever the disease area happens to be whether it's heart disease in the case of what we're doing with NHLBI or whether it's breast cancer or any of the other studies, whether we're talking about just getting the communities to participate in a clinical trial, I think there's a model in Mississippi that ought to be emulated. That is the ability of the institutions in the State of Mississippi to come together and work together.

We've got programs at the Center that are working. The one that you're referring to, the Center for Health Disparities in the State of Mississippi has brought all of the institutions there together. The University of Mississippi Medical Center, Tougaloo College, Jackson State and many other institutions come together to work on these issues. So I believe that irrespective of which disease we're talking about, because health disparities is a very complex issue, it deals with a whole plethora of different disease areas and you have so many experts there who are working on various aspects of this issue.

I think that by bringing these individuals together and everybody working together and understanding where their various strengths and weaknesses are, we're going to get an answer to a number of very important questions here.

Senator COCHRAN. Well, that's very encouraging and we appreciate your hard work and efforts in that regard. Now, you mentioned, was it Dr. Niederhuber or Dr. Fauci, did you have a role—do you have a role in this specifically?

INFORMATION DISSEMINATION

Dr. NIEDERHUBER. Dr. Niederhuber. Dr. N. is easier.

Senator, we as you might imagine at the Cancer Institute track very carefully the hot spots, if you will. We color them red. I don't know if that's significant politically or not but we know where

those hot spots are for various cancers. Some of those areas are industrial; others are what you would call rural.

Appalachia, if you go down through Appalachia we have very high incidence of certain kinds of especially female associated cancers. It's a multiple factorial problem. There's not one simple fix to this. Part of it has to do with education. Some of it has to do with socioeconomic status of those communities.

We look also very carefully at the environment and whether there are environmental relationships that we can pin to risk. We look at the genetic changes in the population to see whether there's a relationship with the genetic background or inherited genetic patterns in those communities that relate to this risk as well.

We're looking at all aspects of it. It's a very complicated issue. Certainly an awful lot of it though has to do with education and an opportunity or access to science, to care.

As I mentioned in my opening statement before you arrived, Senator, we're launching in the next few days actually, 10 pilot centers across the country that are specifically targeted at rural communities. Not universities, but in community environments around community hospitals and probably about 100 to 250 bed facilities. The purpose of those pilots is to try to learn as much as we can about what we're going to need to do to bring the latest of our science, the latest of our discoveries directly to those people.

We know that 85 percent of patients with cancer get the care for their cancer in the community where they live. They don't leave the community. They don't travel to M.D. Anderson in Houston or to Memorial Sloane Kettering or to Duke University or wherever. They stay right at home for a variety of reasons. Part of it has to do with age and the dependency on the family for support and care. That's just what's happening in this country.

We have to understand that better. We have to understand how we're going to get our science, our discovery to people where they live.

Senator COCHRAN. It's very interesting. Well, we thank you for the good work that you're doing. We appreciate your being here at the hearing. We look forward to continuing a close relationship with you as we go through the mark-up process. Thank you.

CANCER SPORE'S PROGRAM

Senator HARKIN. Thank you, Senator Cochran. As I said, Dr. Niederhuber, pancreatic cancer, number four killer among cancers. Once it strikes, very little hope. Senator Stevens had talked a little bit about that. It's one of the few cancers for which mortality rates are virtually the same today as they were 30 years ago. So that makes the work of the three pancreatic cancer SPOREs so important, the Specialized Programs of Excellence.

Dr. NIEDERHUBER. Absolutely.

Senator HARKIN. I understand that NCI is considering changes to the SPORE program that could have a significant impact on pancreatic SPOREs. Could you tell me about your plans in that area?

Dr. NIEDERHUBER. Actually, I think that the changes that we have been making, Senator, have actually strengthened the program. We have been working very hard to keep as much resources,

financial resources into this program as we have had in the past. So we've been scraping to do that.

When I came onboard I looked at some of the struggles and some of the problems. Having come from the academic community and having been Cancer Center Director and knowing a little bit from the outside about the issues that this SPORE program has and how difficult it is to bring the basic scientist together with the clinical scientist. It's not an easy accomplishment for any university to build one of these programs, one of these collaborative efforts.

So I began working directly with the currently funded leadership of the SPORE program across all of the diseases. Some of the things that we decided to do together, collectively, was one to have them come in separately.

Senator HARKIN. Individualized.

Dr. NIEDERHUBER. We would have the lung cancer programs all coming in at the same time but then not being able to come back in for 2 or 3 years for funding. That didn't make a lot of sense to any of us. So we've changed that structure around. We've put in place three separate times a year when anybody who comes together and creates a SPORE program in breast or prostate or pancreatic cancer. They have the resources to put into this and to compete for one of these grants. They can come in September/October or January/February or in the springtime.

They also now have the opportunity, if the study section who reviews that application doesn't give it quite the score to get funding, a score level, they then have the opportunity to immediately respond to that, revise their application and come right back in. That was not something that existed before.

I met with the SPORE PIs about 3 weeks ago at the American Association of Cancer Research meeting in Los Angeles, since they were mostly all there. We had a special opportunity for them to come and sit with me. I reviewed with them the funding plan we have put in place so that they could understand the resources and how the resources were being distributed. They could see the same detail that I have.

I think they really appreciated that. It was the first time that anybody had been that open and shared with them the details of funding. We talked about the future. We talked about some innovative things that we might do with the program that might further enhance the SPORE program.

So I think we have a very collegial working relationship with the research community that's committed to putting these grants together and to keeping them going. The goal is the best science.

Senator HARKIN. I understand but again I think there's some concern that the pancreatic cancer SPOREs will get squeezed out.

Dr. NIEDERHUBER. No. You're talking to a person who's spent his whole life doing pancreatic cancer surgery. So, I'm very committed to being sure we continue that.

PANCREATIC CANCER

Senator HARKIN. One last thing.

Dr. NIEDERHUBER. I'm hopeful that there will be other Institutions that will feel they have the resources, academic, and intellec-

tual resources, to come in. If we get another good application that number is not frozen at three, we'll fund the best we can get.

Senator HARKIN. Ok. One last thing. Pancreatic cancer is so bad because there's no early detection.

Dr. NIEDERHUBER. Correct.

Senator HARKIN. Once you've found out and we all assume we've all had friends die of it. I just had one recently within the last couple of years who was my back seat guy when I flew in the Navy. Literally within, probably, 9 months he was dead.

Dr. NIEDERHUBER. Six months to a year.

Senator HARKIN. I've had others say the same thing. By the time you detect it, it's too late. What kind of hope can you give us? What kind of research is going on for some kind of early detection, methodology for pancreatic cancer?

Dr. NIEDERHUBER. If you remember in my opening presentation I highlighted that. Our genome-wide scanning that we are doing to look at large cohorts of patients to determine what genetic changes may be present in their genome, in their code of DNA, what changes they may carry with them that predict. For example we studied breast first, then prostate. We've learned quite a bit from that.

We've had, I think, over the past 3 months, six papers I believe it is. Don't quote me for sure on that number. But I think it's six papers in Nature which is one of the leading journals as a result of that work in both prostate and breast. So in July of this year we will begin the same kind of study in pancreatic cancer.

I am a person very interested in pancreatic cancer. I'm very excited about that because I think that's the first step in getting the kind of background information we need in terms of what changes may exist in your genome that says you've got a greater risk over your lifetime of developing this kind of cancer. It's a huge step for me, I think, in what we need to know. It will be a great foundation to build on. I hope that out of that we will get some clues of what kind of, we call them biomarkers, to look for in this particular cancer.

TUBERCULOSIS

Senator HARKIN. Thank you very much. Dr. Fauci, I'm hearing more and more about drug resistant tuberculosis. I just had a question on it this weekend from someone. How big is the threat and how prepared are we to deal with it?

Dr. FAUCI. It's a growing threat, Mr. Chairman that we're concerned about. As you know, TB is a very, very important global problem. One third of the world's population is infected with tuberculosis, not sick with it, but infected with it.

Senator HARKIN. One-third of the world's population is infected with tuberculosis.

Dr. FAUCI. One-third of the world's population is infected with tuberculosis, right. We get about 8 million new cases a year with 1.3 to 1.6 million deaths. Twenty percent of all of the tuberculosis active cases are multiple drug resistant. It means that it's resistant to the standard drugs that we use. But we do have alternative drugs. Ten percent of that 20 percent have what we call extensively

drug resistant tuberculosis or XDR as it's referred to. It's a growing problem.

We are ratcheting up very aggressively our tuberculosis portfolio to address the issue of drug resistance. We just, as I mentioned earlier, put together a strategic plan that I presented to my National Advisory Council this morning. Then we will be formalizing that plan. It is a real serious problem.

It was first brought to the attention of the scientific community from about 54 cases that were identified in South Africa, of which an astounding 52 died. That's a very, very high rate. The reason it is likely because they were also co-infected with HIV. It isn't just confined to people with HIV.

But when you say extensively drug resistant you mean that the standard INH and rifampicin, the drugs that you usually give. It's resistant to them. It's resistant to the fluoroquinilones and it's resistant to at least one injectable third-tier tuberculosis drug like amikasin and drugs like that. So it's a very serious problem.

In some cases it is completely non-curable. So we have to work really fast to get other drugs into the pipeline. But importantly to make the right diagnosis because you get drug resistant TB by not properly treating regular TB, and you don't properly treat it because you don't diagnose it early enough. Then when you do, people don't come back for follow-up because they start to feel better right away. So we need to have a good screening process and a very sensitive diagnostic. All of that is part of our strategic plan that I was talking about a moment ago.

MULTIPLE DRUG RESISTANT AND EXTENSIVELY DRUG RESISTANT TB

Senator HARKIN. I think most people would be alarmed to find out tuberculosis which we thought was in the Dark Ages has come back so strongly. I had not known that 1 out of 3, 30 percent. That's alarming.

From the figures that you gave me it's about—you say about 20 percent are multiple drug resistant.

Dr. FAUCI. Ten percent of that 20 percent are extensive.

Senator HARKIN. So 2 percent are resistant to anything.

Dr. FAUCI. Right. Exactly.

Senator HARKIN. Is that in just a certain area of the world? Is that confined to a certain area?

Dr. FAUCI. Thirty-seven countries now have extensively drug resistant tuberculosis. There are a few cases we have in the United States that have been taken care of and contained. The problem is very serious in southern Africa. Interestingly we have a considerable number of cases in the Eastern European bloc countries and even in Korea. But there are 37 countries worldwide that have extensively drug resistant tuberculosis. That's reported.

But given the fact that most of that one-third of the world's population is in the developing world in areas in Asia and India and China and in Africa. That's where you don't likely get the medical care to get the diagnosis to get it treated. So it's a problem that's probably underestimated. So I'm telling you it's 20 percent and then there's 10 percent of 20. It's probably an underestimate as to what's really going on. It's a serious problem.

Senator HARKIN. Is it highly transmissible?

Dr. FAUCI. Well, it's transmissible like any tuberculosis. You need close continued contact and it's aerosolized droplets that contain the tuberculosis bacillus.

Senator HARKIN. Anthrax.

Dr. FAUCI. Yes.

Senator HARKIN. Recent estimates have said we need to be prepared for an anthrax attack. HHS has stockpiled anthrax vaccine and antibiotics. The problem with antibiotics is that they have to be administered shortly after any kind of attack or event. I've heard that there are other therapeutics that could target the toxins released by the anthrax bacteria and therefore could be effective even after the onset of symptoms.

Dr. FAUCI. Correct.

ANTHRAX ANTIBIOTICS AND ANTI-TOXIN

Senator HARKIN. Tell me more about that.

Dr. FAUCI. Sure. We started a program right at the point of a few months after the anthrax attacks here in our capital. One of the concerns we had is that we have very, very good antibiotics for anthrax. In fact, the clinical trial was done among Senate and House staff when they were given Ciprofloxacin following known exposure.

In fact it's very interesting. Some of you may not know that when they did blood test screening of antibodies that many of the people who just did perfectly well because they took Ciprofloxacin or doxycycline. Actually you have proof that they were exposed, which means that if they did not take the antibiotic they very likely would have gotten sick. So the people who took the antibiotics did the really, the right thing about taking the antibiotics. I say that because we have good antibiotics.

But what we are concerned about is, remember, several of the postal workers here in the city who were misdiagnosed initially. Then when they finally had the right diagnosis and were put on Ciprofloxacin, they were so advanced in the disease that the circulating anthrax toxin was the thing that killed them as opposed to the replicating anthrax bacillus.

So, what we've done and we've been rather successful at it is to develop antibodies against the toxin itself. So if you have the antibiotic, prevents the replication of the bacteria, but the anti-toxin neutralizes the circulating toxin which is the thing that actually caused the death of several of those people. So we do have it. Some of it is already in the stockpile and we're working on even better ones.

Senator HARKIN. I was not aware of that.

Dr. FAUCI. Yeah, yeah, it's true.

Senator HARKIN. You actually have it in the stockpile now.

Dr. FAUCI. We have an order for it through Bioshield.

Senator HARKIN. Again this would be effective even after I become symptomatic—after the symptoms arise. You could target that? You say you're working on others, you mean there's——

Dr. FAUCI. There are multiple—there are three major toxins and we have antibodies to all of them. One of the ones, the lethal toxins that are the ones that we're most concerned about. We have now molecular biological techniques where we're trying to make

monoclonal antibodies against. Monoclonal antibodies in anybody you actually code and manufacture to make only the response against a particular toxin you're worried about.

Senator HARKIN. How certain are you? I mean, what's the success rate if you had 100 people who became symptomatic with anthrax and you gave them this vaccine? What's the survival rate?

Dr. FAUCI. It depends when you get it. I have to tell you being an infectious disease person and having taken care of a lot of people who have advanced septicemia and shock. Once a person goes into the toxic septicemia of endotoxic or other types of shock the salvage rate of those individuals is very low.

So I think even with an anti-toxin, if given early enough, before you have a lot amount of accumulated toxin, it would probably increase the salvage rate and decrease the morbidity and mortality significantly. I can't put a number on it for you because the clinical trial has not been done. So it would be folly for me to say, oh it's a 90 percent, 80 percent. We just don't know. We just don't know.

Senator HARKIN. How soon?

Dr. FAUCI. I hope we never have to test it.

Senator HARKIN. How will you know? How will you ever know?

Dr. FAUCI. We'll know when we have another attack.

Senator HARKIN. That's about the only way.

Dr. FAUCI. We have animal models which have worked very, very well in the animal models. But again we always be careful—if you tell me based on the animal model would I project that it would be a success I would say yes. But I have to be very cautious because there's a big leap between a successful animal model and what works in the human.

CANCER STEM CELLS

Senator HARKIN. I've got to go but a couple of things I wanted to cover. Cancer stem cells. There's an idea that within a tumor there are cancer stem cells are really the driving force. That if we could just figure out how to get to those stem cells and target those that we would have a better success rate in curing cancer. What can you tell me about that?

Dr. NIEDERHUBER. Well, it's a very exciting area of research. It is not a totally new concept. It's really an old concept. But it has come back in just the past few years.

An example, Senator Harkin, a year ago at the AACR, the big national research meeting, there were maybe 20, 25 papers. This year there were over 225 papers at the meeting. So it just shows you how the community has become excited and interested in this concept.

So we know that within our tissues, the normal tissues of our body there are cells that are responsible for regenerating those tissues. Let's take the lining of the intestine, the colon, for example. We know that there are what we call tissue stem cells that have a certain division property that allows them to regenerate that lining of the colon.

So the concept is that the genetic changes that occur that lead to a cancer may have to occur in those cells, in those tissue stem cells, in order for the cancer to become a significant lesion—to have the property or potential for invasion and the potential for spread.

In the tumor the bulk of the tumor cells don't carry that kind of genetic imprint.

It's like thinking of the cell as an orchestra. Some of the instruments that give that orchestra in that cell the properties of being stem like in character are in a subpopulation of the tumor, maybe 1 percent, maybe as much as 2 percent of the tumor. The bulk of the cells in the tumor don't have that set of instruments playing at that particular moment.

We think we're doing a good job of getting rid of the bulk of the tumor but what gets left behind is that one percent of cells that can lie quiescent in the tissues of the body for a number of years. Those of us who practice oncology over the years have been always puzzled by seeing a patient with breast cancer seemingly cured 15 years or so later coming back with the disease seemingly everywhere. It may be part of the explanation of this.

So without question we need to learn more about these cells. We need to learn what gives them resistance to the therapies that we use. We know that they have certain properties that can pump drugs that get into the cell immediately back out of the cell. So there are a lot of things that are—that make them more difficult to target. Maybe we haven't been specifically targeting them in the ways that we need to.

Some of the new research is showing pathways that are unique to those cells. That is, signal pathways within the cell and potential ways to target them that are unique. So I think you'll see over the next few years a lot more research going on that is trying to get at that population of cells, better characterizing it and better targeting it for therapy.

NATIONAL PRIMATE RESEARCH CENTERS

Senator HARKIN. Thank you very much. I have a couple of last questions for Dr. Alving. This subcommittee has been very supportive of the primate centers. We included report language in a lot of our past bills, so I was disappointed to see in your budget request that your plans cut the funding for the centers by $1.7 million for a total of $72.3 million. What's the reason for that cut in the primate centers?

Dr. ALVING. This was in the congressional justification estimate and now the fiscal year 2007 joint resolution, which was a higher change from the CJ. But what we have had to do and what we are doing throughout the NCRR is to look at where we can best put our resources.

We are actively working with the primate centers to better manage the consortium. We're saying that they need to work together as a consortium in managing their animal facilities and in managing the breeding of the animals. We're very supportive of the work and they also are working with the CTSAs. So if we have improved funding we will be able to put more money into that program.

Senator HARKIN. Your budget request cut that funding.

Dr. ALVING. This was according to the amount of money that we had allocated as we went across the budget. We will put this money back in. We also are committed——

Senator HARKIN. So, if we—I mean, excuse me for interrupting. So if we do better than the President's budget will you put that money back in?

Dr. ALVING. Yes. Yes, we will.

Senator HARKIN. Ok.

Dr. ALVING. But also realize, Mr. Chairman, that we are working on building up our CTSAs and that's another challenge in NCRR. As we are building the primate centers, we'll be working with the CTSAs. For example, two of our CTSA awardee institutions, Oregon and UC Davis have primate centers. Those primate centers are working in that consortium as well.

But we are very supportive of the primate centers. They're doing excellent work. I visited four out of eight of them. We want to work with them as a consortium to support them.

GCRC TRANSITION INTO CTSA

Senator HARKIN. Ok. Well we'll try to put some more money in there for it. It's not that big. One last question on the CTSAs. As you say you're building them up, but what happens to the General Clinical Research Centers? I guess they're going to be folded into them or something like that?

Dr. ALVING. There will be a transition into the Clinical and Translational Science Awards. For example, of the first 12 CTSA awards that were provided, 16 General Clinical Research Centers were included. Those have become part of the CTSAs.

We're also emphasizing pediatrics in the CTSAs. For example, at the University at Pennsylvania, two General Clinical Research Centers were folded into that CTSA award, one from the Children's Hospital of Pennsylvania, one from the University of Pennsylvania. Now they are absolutely working together.

Senator HARKIN. So you can assure me there will be no diminution of training researchers the next generation in translation and clinical research because of this new structure.

Dr. ALVING. What we're really building is the training of the clinical researchers because the GCRC program never included training. So this is a big component of the new CTSAs.

Senator HARKIN. Thank you. Any last things from anyone else that I didn't touch on or that you wanted to express yourself on before I gavel this closed here? I thought it was a very good hearing. I think we got a lot out and a lot of good information.

Again, I thank you all very much for your leadership in all these various areas. I just hope that we can get a little bit better budget than what the President requested. We will. We'll get better than what the President requested. And now we're looking ahead to see how we can repair some of the damage of the last few years. The 12 percent or 13 percent that we've come down in NIH over the last 4 or 5 years and we've got to get it back up again. But that's our problem. We'll see if we can do better on that.

So with that, thank you very much. We have one more group from NIH and we haven't scheduled a hearing but I assume it won't be this week and it won't be next week because we're not here. So it will be sometime in June we'll have the last set of hearings.

ADDITIONAL COMMITTEE QUESTIONS

So I thank you very much and we will keep the record open for any questions that other Senators who weren't here today have for you that they might submit in writing.

[The following questions were not asked at the hearing, but were submitted to the Department for response subsequent to the hearing:]

QUESTIONS SUBMITTED BY SENATOR TOM HARKIN

FOOD ALLERGIES AND ANAPHYLAXIS

Question. Dr. Fauci, children who have had atopic dermatitis, also known as eczema, are more likely to have severe food allergies and asthma. Has the NIAID considered the possibility of funding a complementary initiative, perhaps in coordination with the NHLBI, on atopic dermatitis as it relates to asthma and food allergy?

Answer. The National Institute of Allergy and Infectious Diseases (NIAID) is committed to supporting research to better understand the relationship of atopic dermatitis (AD) to asthma and other allergic diseases, particularly food allergy. At this time, the NIAID is supporting several studies in this area. The Consortium of Food Allergy Research is conducting an observational study of the development and loss of tolerance to foods in a cohort of 400 children, ages three to twelve months, at a high risk of developing food allergies, including children with AD. The study will correlate biological markers and immunologic changes associated with the development of peanut allergy and the resolution of allergies to egg and cow's milk, and evaluate genetic and environmental influences on these food allergies.

Another NIAID-sponsored program, the Immune Tolerance Network, is conducting two clinical trials related to food allergy and AD. The first will determine whether feeding a peanut-containing snack to young children at risk of developing peanut allergy will prevent development of this allergy. The subjects are children between 4 and 10 months of age with AD and/or allergy and they will be followed until they reach 5 years of age. The second clinical trial is enrolling children with AD who are between the ages of 18 and 30 months and at high risk for developing allergies. This trial will determine whether oral administration of cat, grass, and house dust mite allergens will prevent the development of allergy to these and other allergens and asthma in these children.

The NIAID Inner-City Asthma Consortium is conducting the Urban Environment and Childhood Asthma (URECA) observational study, which will assess antibodies to milk, egg white, and peanut in infants at risk for developing allergic diseases, including asthma, allergic rhinitis, and AD. The study will look for a correlation between food allergies and the onset of asthma later in life.

Lastly, the NIAID currently collaborates with NHLBI on two initiatives related to asthma. One of these, Immune System Development and the Genesis of Asthma, includes a grant which studies the relationship of AD to asthma.

Question. What plans does NIAID have to encourage research applications on anaphylaxis? Has the NIAID considered the need for clinical studies of emergency room treatment for anaphylaxis?

Answer. To address the problem of anaphylaxis, the NIAID is pursuing two major approaches: expanding support for research on the causes, treatment, and prevention of allergic diseases, including food allergies and food-allergy-induced anaphylaxis; and supporting national and international conferences that will disseminate new knowledge and promote a more cohesive approach to the diagnosis, prevention, and clinical management of anaphylaxis.

Expanding research

—The Report of the NIH Expert Panel on Food Allergy Research discussed food-induced anaphylaxis in detail and emphasized the need to study the pathogenesis of severe food allergy.

—The NIAID-funded Consortium of Food Allergy Research is conducting an observational study of the natural history of food allergy, which is expected to provide new information about severe allergic reactions and anaphylaxis. In addition, the Consortium is conducting a clinical trial focused on severe food allergy, which will use increasing oral doses of egg to treat patients with severe egg allergies.

—The NIAID has just announced a new initiative, Exploratory Investigations in Food Allergy, which encourages studies on severe life-threatening food allergy.

Supporting national and international conferences

—The NIAID, in partnership with the Food Allergy and Anaphylaxis Network (FAAN), a patient advocacy group, convened meetings in 2004 and 2005 to establish clinical criteria to identify cases of anaphylaxis with high precision, review evidence on the most appropriate clinical management of anaphylaxis, and outline research needs in this area. Participants included experts and representatives from professional, governmental, and lay organizations. The proceedings of these symposia were published in the March 2005 and February 2006 issues of the Journal of Allergy and Clinical Immunology.

The NIH Expert Panel on Food Allergy Research considered the need for clinical studies of emergency room treatment for anaphylaxis and presented its recommendations as part of its report.

Question. Does NIAID make information available to health professionals about the best approaches to treating food allergy?

Answer. The Consortium of Food Allergy Research was initiated in 2005 to develop new approaches to treat and prevent food allergies. As such, one of the goals of the Consortium is the development, implementation, and dissemination of educational programs for children, their parents, and pediatric health care workers. In addition, the Consortium supports preclinical research, observational studies, and immune-based clinical trials for treatment or prevention of food allergies.

To ensure that the information on diagnosis, prevention and management of anaphylaxis is developed and widely disseminated to the medical community, NIAID, in collaboration with FAAN and the American Academy of Allergy, Asthma and Immunology, is organizing a series of meetings. These are scheduled to begin in July 2007 and will develop evidence-based guidelines for the diagnosis and management of food allergy, including anaphylaxis.

TOBACCO-RELATED RESEARCH

Question. Dr. Niederhuber, in March, you told NCI's Board of Scientific Advisors that the Tobacco Control Research Branch has been cut by $6.5 million between fiscal year 2004 and fiscal year 2007. Are those numbers still correct? If so, can you tell us how cutting back on this type of research will affect our ability to prevent tobacco-related cancers?

Answer. The Tobacco Control Research Branch (TCRB) budget was $19.2 million in fiscal year 2004. We are still in the process of making final funding decisions, but the current estimate for fiscal year 2007 is $12.7 million, which is a reduction of $6.5 million from fiscal year 2004. Part of the reduction during the period between fiscal year 2004 and fiscal year 2007 was due to the expiration of some tobacco control research initiatives. However, additionally, the period following the doubling of the NIH budget has resulted in very difficult choices in terms of setting priorities and implementing funding decisions. The NCI Executive Committee and advisory boards have worked diligently to conduct strategic priority setting and decision making related to the scientifically appropriate distribution of resources. In order to pursue new and emerging opportunities in cancer research, we must make choices about which programs and research initiatives come to an end.

In terms of planning for the future, scientists in TCRB are currently working on several new research concepts in response to the 2006 NIH State of the Science Conference, "Tobacco Use: Prevention, Cessation and Control," and other priority setting reports. NCI will use these concepts to develop and redirect initiatives in tobacco control research in the future.

NCI's research efforts in the prevention and control of tobacco use are premised on three fundamental facts: all tobacco products are hazardous; there is no safe level of tobacco use or ETS exposure; and the only proven way to reduce the burden of disease and death due to tobacco products is to prevent their use and to assist those who use tobacco products to quit. Further progress in reducing tobacco use is an important challenge facing the public health, medical, and policy communities.

The Tobacco Control Research Branch (TCRB) maintains a diverse portfolio of research and dissemination activities. Most noteworthy are the following:

—Transdisciplinary Tobacco Use Research Centers (TTURC). The TTURCs are a collaboration between NCI, NIDA, and NIAAA to study tobacco use control and addiction research spanning diverse areas ranging from molecular biology, genetics, neuroscience, and epidemiology to imaging, primary care, behavioral science, communication, health policy, biostatistics, economics, and marketing. Collaborative research across disciplinary boundaries permits scientific exploration of the complex and interactive determinants of tobacco use.

—Testing Tobacco Products Promoted to Reduce Harm is a program which funds multidisciplinary research on the interplay of behavior, chemistry, toxicology,

and biology to determine the cancer risk potential of reduced-exposure tobacco products.

—Smokefree.gov is a state-of-the-art Web site developed by NCI in collaboration with the Centers for Disease Control and Prevention (CDC) and the American Cancer Society (ACS). It offers science-based tools and support to help smokers quit. Smokefree.gov complements the National Quitline Network that has established a new state-supported national telephone number so smokers in every state have access to information and proactive smoking cessation counseling.

—The Health Disparities Network is a unique endeavor to understand and address tobacco-related health disparities by advancing science, translating scientific knowledge into practice, and informing public health policy. In partnership with the Pennsylvania State University, core scientific activities are focused on methodology, treatment/cessation, prevention, translation/community, and policy. The formation of the network fills a void by establishing a mechanism to bring together an ethnically diverse group of researchers representing different disciplines and interests to answer multiple questions related to the research agenda in health disparities and explore optimal mechanisms for translating research into practical and effective community strategies.

MINORITY HEALTH

Question. Dr. Ruffin, if the Subcommittee were able to provide additional funding for the Center over the President's budget request, what would be your top priority for how to spend it (e.g., health disparities research vs. research capacity-building and infrastructure), and why? Please be as specific as possible.

Answer. The fiscal year 2008 President's Budget request of $194.5 million will support NCMHD's highest priority research activities. However, if the NCMHD were to receive any additional funding over the President's budget request, those funds would go towards research capacity-building specifically in the area of training. Having a strong and culturally diverse workforce is vital to the ability of NCMHD to fulfill its mission to improve minority health and eliminate health disparities. NCMHD would place additional emphasis on recruitment and retention at every level of the pipeline.

First, NCMHD would strengthen the retention component of the NCMHD Loan Repayment Program in order to keep more individuals from health disparity populations interested and involved in health disparities research, as well as attract young investigators from these populations to the biomedical research field in general.

Second, NCMHD would be to further develop the capacity of our Centers of Excellence to enhance their capability in conducting research into the multi-factorial issues associated with health disparities. The research efforts of these Centers contribute significantly in enhancing the nation's understanding of health disparities, and offer the training and professional research environment required for the workforce to study minority health and health disparities issues.

FOOD ALLERGIES

Question. Dr. Fauci, during the hearing, you indicated that the "roadmap" which was developed by the leading food allergy researchers and experts in immunology after they met in March 2006 is still in the process of being approved. When will it likely be released?

Answer. In March 2006, the National Institute of Allergy and Infectious Diseases (NIAID), on behalf of the Secretary of the Department of Health and Human Services, convened the NIH Expert Panel on Food Allergy. The Expert Panel met to review current basic and clinical research on food allergies and develop recommendations for enhancing and coordinating research activities concerning food allergies. The recommendations have now been posted on the NIAID website at http://www3.niaid.nih.gov/healthscience/healthtopics/foodAllergy/ReportFoodAllergy.htm.

QUESTIONS SUBMITTED BY SENATOR DANIEL K. INOUYE

NATIVE HAWAIIANS AND CANCER

Question. Dr. Niederhuber, Native Hawaiians have a much higher mortality rate from cancer than other residents of the State. What efforts has the National Cancer Institute taken to understand cancer in Native Hawaiians?

Answer. The National Cancer Institute (NCI) continues to support research to find the causes of cancer health disparities and to develop effective ways to improve cancer outcomes for Native Hawaiians. Among these continued efforts are: enhanc-

ing surveillance of Native Hawaiian populations to document the extent of cancer health disparities and monitor progress in improving cancer outcomes in these communities; empowering Native Hawaiian communities to participate in setting cancer research goals and priorities; assuring access to community-based health care that is culturally and linguistically appropriate; supporting infrastructure for Native Hawaiian communities that promotes cancer awareness, supporting research education and training in cancer prevention and control research by Native Hawaiian researchers, and supporting the development of evidence-based information and interventions to improve cancer outcomes in Native Hawaiian communities.

Community Networks Program

Two of NCI's Community Networks Programs continue to address Native Hawaiian populations: 'Imi Hale—Native Hawaiian Cancer Network, and WINCART: Weaving an Islander Network for Cancer Awareness, Research and Training. These five-year grants, engage in cancer education, community-based participatory research and training targeted specifically to the Native Hawaiian population.

The Native Hawaiian Cancer Network, 'Imi Hale, is located in Honolulu, Hawaii and collaborates with key partners at the community, state, and national levels to provide support systems and expertise to: (1) provide a core organizational infrastructure; (2) increase utilization of proven interventions to reduce disparities; (3) increase the number of Native Hawaiians participating in community-based research to reduce cancer health disparities through recruitment, training, and mentorship; (4) promote research that focuses on the spectrum of issues relevant to cancer health disparities, with an emphasis on developing interventions that can be used in and by Native Hawaiian communities; and (5) provide evidence-based information on reducing cancer health disparities to decision and policy makers at the community, local, state, and Federal levels.

WINCART

WINCART aims to: (1) identify multilevel barriers to cancer control among Pacific Islanders; (2) improve access to and utilization of existing cancer prevention and control services for these communities; (3) conduct community-based participatory research; (4) increase the number of Pacific Islander researchers through training, mentorship, and research projects; (5) sustain community-based education, training, and research activity through government and organizational collaborations; and (6) disseminate research to aid in the reduction of health disparities among Pacific Islander communities. Research activities focus on obesity, tobacco, cancer screening, survivorship, and recruitment of Pacific Islanders into clinical trials. The Network works with the NCI-supported Cancer Information Service to develop culturally and linguistically appropriate educational materials.

NCI SURVEILLANCE OF CANCER HEALTH IN NATIVE HAWAIIAN POPULATIONS

NCI continues to strengthen the Surveillance Epidemiology and End Results (SEER) Program which has expanded its surveillance coverage and activities to capture 70 percent of Native Hawaiians and Pacific Islanders in the surveillance network. These include cancer surveillance, behavioral risk factor surveillance, health information and health services data, and epidemiologic data. This expansion is critical to uncovering the extent of the cancer problem and monitoring progress in eliminating cancer disparities in Native Hawaiian and Pacific Islander communities.

CANCER IN PACIFIC ISLAND SUBPOPULATIONS

The NCI also recognizes the dramatic disparities found in many Pacific Island subpopulations, including rural Native Hawaiian populations. Through the Minority Institution/Cancer Center Partnership Program, NCI supports a research partnership between the University of Guam, and the Hawaii Cancer Research Center to address the cancer research needs of Guam and adjoining Islands.

Through the Cancer Information Service, NCI supports efforts to provide NCI products, resources and services, including promotion of the Clinical Trials Education Series and clinical trials to individual hospitals in Hawaii approved through the American College of Surgeons Commission on Cancer (ACoS). In addition, CIS provides professional training in cancer and cancer clinical trials throughout Hawaii, raises awareness among Kauai Community College (KC) nursing students about cancer clinical trials, and promotes access and dissemination of NCI cancer clinical trials resources. These efforts have improved screening rates among Hawaii's medically underserved populations.

NURSING

Question. Dr. Grady, could you discuss the funding rates of the NINR compared to other institutes at the NIH? What percentage of nursing studies are co-funded with other institutes? What are your impressions of co-funded studies?

Answer. NINR, like the rest of NIH, calculates success rates by dividing the number of research project grant (RPG) applications selected for funding in a given fiscal year by the total number of RPG applications reviewed during that year. In fiscal year 2006, NINR had a success rate of 18 percent, slightly lower than the overall rate of 20 percent for NIH as a whole. NINR has historically had success rates lower than the NIH average; however, success rates can and do fluctuate from one year to another based on both the number of applications received and the overall NINR budget. In fiscal year 2006, NINR chose to devote about 72 percent of its budget to the support of RPGs.

In fiscal year 2006, approximately 7 percent of NINR-supported research grants were co-funded by one or more of the other NIH Institutes and Centers (ICs). However, co-funding is only one aspect of NINR's overall collaborative effort across NIH. In today's increasingly complex, interdisciplinary research environment, NINR views trans-NIH collaborations as an important part of its research mission. In addition to co-funding research, other such efforts include: co-sponsoring new research initiatives with other ICs, leading the NIH effort in end-of-life research, and maintaining leadership roles in trans-NIH activities such as the NIH Pain Consortium, Public Trust Initiative, and Roadmap. Greater collaboration with other ICs increases both the visibility of nurse scientists in the greater research community and trans-NIH awareness of research areas traditionally associated with nursing science, such as symptom management and disease prevention. Interdisciplinary collaborations also provide our own investigators with opportunities to expand the breadth of their work into areas of research not previously associated with nursing science.

NIAID AND NATIVE HAWAIIANS

Question. Dr. Fauci, in your testimony, you indicate that autoimmune diseases, allergic diseases, asthma and other immune-mediated diseases are significant causes of chronic disease and disability in the United States and throughout the world. With respect to asthma and lower respiratory disease, Native Hawaiian adults have a much higher prevalence of asthma compared to other adults in Hawaii—71 percent higher than the total State prevalence. How can the NIAID contribute to a greater understanding of the asthma among Native Hawaiians?

Answer. Native Hawaiians, along with other minority U.S. populations, have higher asthma prevalence. A recent Centers for Disease Control and Prevention report indicates that the prevalence of asthma in children in Hawaii, is among the highest in the Nation. The National Institute of Allergy and Infectious Diseases (NIAID) welcomes research grant applications focusing on the causes of increased asthma prevalence and morbidity. While the NIAID is not currently supporting research that investigates asthma in Native Hawaiians, the Institute is actively supporting research in other groups who have high asthma prevalence and morbidity.

One of the Institute's initiatives is the Inner City Asthma Consortium (ICAC), which aims to identify the causes for increased asthma prevalence and morbidity and develop effective management approaches in urban, minority children populations.

Additionally, the NIAID and the National Heart, Lung, and Blood Institute (NHLBI) co-sponsor the "Immune System Development and the Genesis of Asthma" program, which supports research on changes in immune function that occur early in life and lead to the development of asthma.

Information gained from these studies will enhance our understanding of the mechanisms of increased asthma in specific populations. We hope that this understanding can be extended to Native Hawaiians and can lead to measures of prevention and therapy that will ameliorate this significant health problem.

DENGUE FEVER

Question. Dr. Fauci, in 2001, Hawaii experienced an outbreak of dengue fever that lasted 8 months, in which over 1,500 people experienced severe sickness. Worldwide, dengue fever kills approximately 25,000 each year, and it is estimated that there are between 50 million and 100 million cases of dengue fever illness each year. Given the impact of this disease on my constituents, what efforts has the NIAID taken towards vaccine development?

Answer. The National Institute of Allergy and Infectious Diseases (NIAID) is currently supporting several research projects to develop a safe and effective vaccine against dengue fever. Development of a dengue vaccine is challenging because of several factors, chiefly, the requirement that a dengue vaccine be tetravalent, that is, simultaneously protective against all four dengue serotypes. Researchers at the NIAID have developed components of a tetravalent dengue vaccine that are undergoing clinical testing. Other efforts to develop a vaccine against dengue fever include support of the following research projects:

—Preclinical and clinical development of a recombinant subunit vaccine against the 4 dengue serotypes (Hawaii Biotech, Inc., Aiea, HI): Additional formulation studies and toxicology testing are currently ongoing in preparation for a Phase I clinical trial planned for 2008.

—Preclinical development of live attenuated vaccine against the 4 dengue serotypes (InViragen, LLC., Mount Horeb, WI): Extensive safety and efficacy testing is currently being conducted in different animal models in preparation for a Phase I clinical trial.

—Development of a microneedle array system for delivery of a DNA tetravalent dengue vaccine in the skin (Cyto Pulse Sciences, Glen Burnie, MD): This vaccine is currently being tested for immunogenicity in different animal models, and the microneedle array will be tested in human volunteers for safety.

—Development of dengue virus replicon system to measure dengue virus neutralizing antibodies in the serum (Integral Molecular, Philadelphia, PA): This assay will be evaluated using serum samples of patients who are hospitalized with dengue fever in Nicaragua.

—Recombinant envelope protein domain III as a candidate subunit dengue vaccine (University of Texas Medical Branch, Galveston, TX): The long-term goal of this project is the development of a candidate subunit vaccine that induces neutralizing antibodies for all four flaviviruses that cause dengue fever.

Question. When may we expect to have an effective product?

Answer. The candidate vaccines listed previously are moving through the product development pipeline. However, the challenges facing the development of a safe and effective vaccine are still significant. The timeline for a vaccine product to be manufactured for use in the United States depends upon a manufacturer successfully completing late-stage clinical trials, including a Phase IV population effectiveness trial and submitting the results to the Food and Drug Administration for licensure. This can be a lengthy process and can extend several years after clinical trials have been completed.

Question. Which other States may be affected in the near future?

Answer. According to the Centers for Disease Control and Prevention (CDC), there is a small risk for dengue outbreaks in the continental United States. However, the epidemic in Hawaii in 2001 serves as a reminder that many states in the United States are susceptible to dengue epidemics. In particular, states in southern and southeastern United States, where the Aedes aegypti mosquito is found, are at risk for dengue transmission and sporadic outbreaks (http://www.cdc.gov/ncidod/dvbid/dengue/index.htm).

Question. What impact, if any, could global warming have on the spread of dengue-carrying mosquitoes?

Answer. Environmental events, such as climate shifts, weather changes, and deforestation, can affect infectious diseases, particularly vector-borne diseases such as dengue virus. High temperatures, in combination with favorable rainfall patterns, could prolong the disease transmission season in places where the virus already exists or expand the ranges of the mosquito vectors to places where the disease is not usually found, such as Hawaii and the southern region of the continental United States.

TERRORISM PREPAREDNESS

Question. Dr. Fauci, the NIAID has been assigned the responsibility to coordinate research to develop countermeasures against a range of radiological and chemical threats. You describe how the Centers for Medical Countermeasures against Radiation coordinate activities with interagency partners, including the Department of Defense, Department of Energy, and Department of Homeland Security. Could you describe ongoing research of medications that would provide protection against radiation in the event of a small nuclear weapon or a dirty bomb?

Answer. The National Institute of Allergy and Infectious Diseases (NIAID) is currently evaluating multiple compounds, including many drugs that are licensed for other indications, for use as countermeasures to combat the effects of an incident involving release of radioactive material. This research is part of the NIAID radi-

ation and nuclear countermeasures program, which is guided by the NIH Strategic Plan and Research Agenda for Medical Countermeasures Against Radiological and Nuclear Threats.

Examples of specific NIAID-supported research initiatives include:

—Research on all elements of radiation injury and the development of products that can be licensed and included in the Strategic National Stockpile.

—Programs to screen candidate compounds for use as radiation countermeasures. These programs have tested 40,000 compounds and identified 52 for further evaluation.

—Development of improved forms of the chelating agent diethylenetriaminepentaacetic acid (DTPA). A chelating agent is a compound that binds to a radionuclide and facilitates and accelerates its elimination from the body.

—Research on 29 candidate drugs that exhibit activity against a broad range of radionuclides that might be used in radiological dispersion devices or "dirty bombs", including several that currently lack effective treatment approaches, such as Strontium 90 and Cobalt 60.

Research to develop medical countermeasures to treat radiation injury remains in the early stages of development; significant research and pre-clinical testing is needed before we will have candidate products developed to treat radiation injury that can move forward for licensure.

QUESTION SUBMITTED BY SENATOR ARLEN SPECTER

OVARIAN CANCER

Question. Dr. Niederhuber, as you are aware, there is currently no early detection method for ovarian cancer. Because of this, more than 75 percent of women diagnosed with ovarian cancer die within five years of being diagnosed. If we were to find these cancers early, the mortality rate falls dramatically to about 15 percent. And, ovarian cancer is not alone; similar statements could be made for pancreatic cancer. Please share NCI's strategy for fiscal year 2008 regarding early detection research, such as biomarkers, for cancers like ovarian and pancreatic, where the incidence numbers are smaller than, say, breast or prostate cancer, but the mortality rates are much higher.

Answer. NCI launched the Pancreatic Cancer Cohort Consortium (PanScan), which is conducting whole genome scans of common genetic variants in 1,200 pancreatic cancer cases and 1,200 controls from 12 cohorts to identify markers of susceptibility to pancreatic cancer. The promising genetic variants (single nucleotide polymorphisms (SNPs) identified will be validated by testing data from participants in a pancreatic cancer case-control consortium. It is anticipated that SNPs that are highly likely to be markers for genetic variants related to pancreatic cancer risk will emerge from this analysis as they have in similar studies on prostate and breast cancers, and lead to further studies of gene-gene and gene-environment interactions with pancreatic cancer risk factors. It is hoped that the PanScan will lead to identification of not only susceptibility genes but early markers for disease. This would be particularly useful for pancreatic cancer which is usually diagnosed at an advanced stage.

There are also several projects being conducted on ovarian and pancreatic cancer in NCI's Early Detection Research Network (EDRN). Scientists are conducting research to enhance early detection of ovarian cancer. EDRN plans to screen serum DNA from larger cohorts of early ovarian cancer patients and controls collected by the EDRN- and SPORE-funded clinical centers for validating the optimized panel of genes for early detection and risk assessment. There are also a number of similar studies to discover biomarkers for the early detection of pancreatic cancer.

NCI launched a unique program in September 2006, the NCI's Clinical Proteomic Technologies Initiative (CPTI). CPTI represents a highly-organized approach to apply proteomic technologies and data resources to support the discovery of biomarkers for the early detection of cancer and to monitor therapeutic outcomes. CPTI will advance the field of clinical cancer proteomics through the development of an integrative team framework that networks multiple research laboratories to permit large-scale, real-time exchange and application of existing and newly developed protein measurement technologies, biological resources, and data dissemination. Efforts will include refining and standardizing technologies, reagents, methods, and analytic platforms in order to ensure reliable and reproducible identification, quantification, and validation of proteins from complex biological mixtures; and evaluating

new technological approaches to identify proteins that occur during cancer development.

In December 2005, leaders from NCI and the National Human Genome Research Institute (NHGRI) launched The Cancer Genome Atlas (TCGA) Pilot Project, a comprehensive effort to accelerate understanding the molecular basis of cancer, and was the result of a "blue-ribbon" committee of the nation's leading scientists. Cancer includes more than 200 different diseases, each with a set of genetic changes that results in uncontrolled cell growth. The purpose of the Cancer Genome Atlas pilot is to test the feasibility of completely sequencing and cataloging the full range of genetic defects in 3 tumor types—brain (glioblastoma), lung and ovarian cancers, leading the way to a better understanding of all cancers.

SUBCOMMITTEE RECESS

Senator HARKIN. Thank you all very much. The subcommittee will stand in recess.

[Whereupon, at 4:10 p.m., Monday, May 21, the subcommittee was recessed, to reconvene at 10 a.m., Friday, June 22.]